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BY

DR L. LANDOIS,

PROFESSOR OF PHYSIOLOGY AND DIRECTOR OF THE PHYSIOLOGICAL INSTITUTE,
UNIVERSITY OF GREIFSWALD.

TRANSLATED FROM THE SEVENTH GERMAN EDITION.

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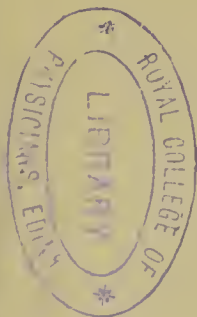
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TO

SIR JOSEPH LISTER, BARONET,

M.D., D.C.L., LL.D., F.R.SS. (LOND. AND EDIN.),

PROFESSOR OF CLINICAL SURGERY IN KING'S COLLEGE, LONDON; SURGEON-EXTRAORDINARY TO THE QUEEN
FORMERLY REGIUS PROFESSOR OF CLINICAL SURGERY IN THE UNIVERSITY OF EDINBURGH.

IN ADMIRATION OF

The Man of Science,

WHOSE BRILLIANT DISCOVERIES HAVE REVOLUTIONISED
MEDICAL PRACTICE, AND CONTRIBUTED INCALCULABLY TO THE

WELL-BEING OF MANKIND ;

AND IN GRATITUDE TO

The Teacher,

WHOSE NOBLE EARNESTNESS IN INCULCATING

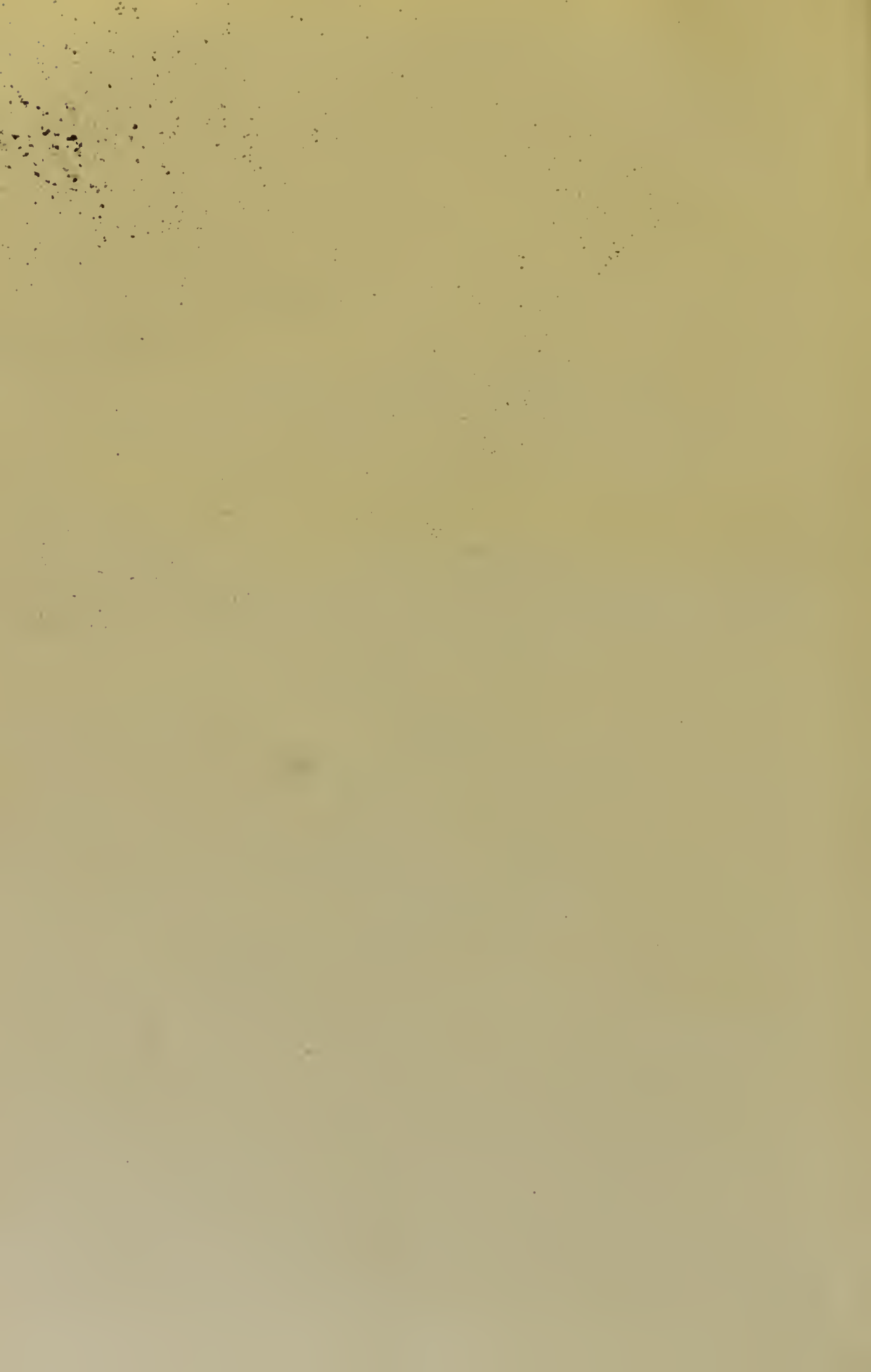
THE SACREDNESS OF HUMAN LIFE

STIRRED THE HEARTS OF ALL WHO HEARD HIM :

This Work is respectfully Dedicated

BY HIS FORMER PUPIL,

THE TRANSLATOR.



PREFATORY NOTE TO FOURTH ENGLISH EDITION.

THE FOURTH English Edition of the Text-book now laid before the Profession has again been thoroughly revised, so as to bring every Section as far as possible into harmony with the most recent advances in Physiological Science.

A new feature introduced—that of printing some of the illustrations of Microscopical subjects in Colours—will, it is hoped, be found helpful. For drawing several of these coloured figures I am indebted to Arthur Clarkson, M.B., C.M., formerly my junior Demonstrator of Physiology, and for others to my pupils, Mr V. E. H. Lindesay and Mr F. J. S. Mathwin.

A large number of new figures, many of them original, have also been added, so that the total number of illustrations is now 845. My acknowledgments are due, specially, in regard to some of these, to the Cambridge Scientific Instrument Company, Messrs Alvergnyat, Verdin, Petzold, Curry & Paxton, and to my friends Professors Roy, Fredericq, Leech, Burdon-Sanderson, Mr Gotch, Dr Adami, and Dr Macnaughton Jones.

Further, I have to thank the last mentioned for some hints which have enabled me to improve the Section on the “Ear and Hearing.” I am also indebted to Professor Ramón y Cayal, of Barcelona, for his courtesy in sending me his original Papers recording the results of his investigations on the Central Nervous System, some of which I have ventured to epitomise and introduce into the text. The sources of the other illustrations are given elsewhere.

In order to do full justice to the coloured illustrations, and to admit of more of the text being printed in large type, it has been found necessary to issue the work once again in two volumes.

WILLIAM STIRLING.

THE OWENS COLLEGE, MANCHESTER,
May 1891.

PREFACE TO THE FIRST ENGLISH EDITION.

THE fact that Professor LANDOIS' "*Lehrbuch der Physiologie des Menschen*" has already passed through Four large Editions since its first appearance in 1880, shows that in some special way it has met the wants of Students and Practitioners in Germany. The characteristic which has thus commended the work will be found mainly to lie in its eminent *practicality*; and it is this consideration which has induced me to undertake the task of putting it into an English dress for English readers.

Landois' work, in fact, forms a *Bridge* between Physiology and the Practice of Medicine. It never loses sight of the fact that the Student of to-day is the practising Physician of to-morrow. Thus, to every Section is appended—after a full description of the normal processes—a short *résumé* of the pathological variations, the object of this being to direct the attention of the Student, from the outset, to the field of his future practice, and to show him to what extent pathological processes are a disturbance of the normal activities.

In the same way, the work offers to the busy physician in practice a ready means of refreshing his memory on the theoretical aspects of Medicine. He can pass *backwards* from the examination of pathological phenomena to the normal processes, and, in the study of these, find new indications and new lights for the appreciation and treatment of the cases under consideration.

With this object in view, all the methods of investigation which may with advantage be used by the Practitioner, are carefully and fully described; and Histology, also, occupies a larger place than is usually assigned to it in Text-books of Physiology.

A word as to my own share in the present version:—

(1.) In the task of translating, I have endeavoured throughout to convey the author's meaning accurately, without a too rigid adherence to the original. Those who from experience know something of the difficulties of such an undertaking will be most ready to pardon any shortcomings they may detect.

(2.) Very considerable additions have been made to the Histological, and also (where it has seemed necessary) to the Physiological sections. All such additions are enclosed within square brackets []. I have to

acknowledge my indebtedness to many valuable Papers in the various Medical Journals—British and Foreign—and also to the Histological Treatises of Cadiat, Ranvier, and Klein; Quain's *Anatomy*, vol. II., ninth edition; Hermann's *Handbuch der Physiologie*; and the Text-books on Physiology by Rutherford, Foster, and Kirkes; Gamgee's *Physiological Chemistry*; Ewald's *Digestion*; and Roberts's *Digestive Ferments*.

(3.) The illustrations have been greatly increased in number, viz., from 275 in the Fourth German Edition to 494 in the English version. These additional Diagrams, with the sources whence derived, are distinguished in the List of Woodcuts by an asterisk.

There only remains for me now to express my thanks to all who have kindly helped in the progress of the work, either by furnishing Illustrations or otherwise—especially to Drs Byrom Bramwell, Dudgeon, Lauder Brunton, and Knott; Mr Hawksley; Professors Hamilton and M'Kendrick; to my esteemed teacher and friend, Professor Ludwig, of Leipzig; and finally, to my friend, Mr A. W. Robertson, M.A., formerly Assistant Librarian in the University, and now Librarian of the Aberdeen Public Library, for much valuable assistance while the work was passing through the press.

In conclusion—and forgetting for the moment my own connection with it—I heartily commend the work *per se* to the attention of Medical Men, and can wish for it no better fate than that it may speedily become as popular in this country as it is in its Fatherland.

WILLIAM STIRLING.

ABERDEEN UNIVERSITY,

November 1884.

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Introduction.

The Scope of Physiology and its Relation to other Branches of Natural Science.

PHYSIOLOGY is the science of the vital phenomena of organisms, or, broadly, it is the Doctrine of Life. Corresponding to the classification of organisms, we distinguish—(1) *Animal Physiology*; (2) *Vegetable Physiology*; and (3) the *Physiology of the Lowest Living Organisms*, which stand on the border line of animals and plants, *i.e.*, the so-called *Protistæ* of Haeckel, micro-organisms, and those elementary organisms or *cells* which exist on the same level.

The object of Physiology is to establish these phenomena, to determine their regularity and causes, and to refer them to the general fundamental laws of Natural Science, *viz.*, the Laws of Physics and of Chemistry.

The following Scheme shows the relation of Physiology to the allied branches of Natural Science:—

BIOLOGY.

The science of organised beings or organisms (animals, plants, protistæ, and elementary organisms).

I. Morphology.

The doctrine of the **form** of organisms.

General Morphology.	Special Morphology.
The doctrine of the formed elementary constituents of organisms.	The doctrine of the <i>parts and organs</i> of organisms.
(Histology)—	(Organology)—
(a) Histology of Plants.	(a) Phytotomy.
(b) Histology of Animals.	(b) Zootomy.

II. Physiology.

The doctrine of the **vital phenomena** of organisms.

General Physiology.	Special Physiology.
The doctrine of vital phenomena in general—	The doctrine of the activities of the individual organs—
(a) Of Plants.	(a) Of Plants.
(b) Of Animals.	(b) Of Animals.

III. Embryology.

The doctrine of the **generation and development** of organisms.

<i>Morphological part</i> of the doctrine of development, <i>i.e.</i> , the doctrine of <i>form</i> in its stages of development— (a) General. (b) Special.	1. History of the development of <i>single</i> beings, of the individual (<i>e.g.</i> , of man) from the ovum onwards (Ontogeny)— (a) In Plants. (b) In Animals.	<i>Physiological part</i> of the doctrine of development, <i>i.e.</i> , the doctrine of the <i>activity</i> during development— (a) General. (b) Special.
	2. History of the development of a <i>whole stock</i> of organisms from the lowest forms of the series upwards (Phylogeny)— (a) In Plants. (b) In Animals.	

Morphology and Physiology are of equal rank in biological science, and a previous acquaintance with Morphology is assumed as a basis for the comprehension of Physiology, since the work of an organ can only be properly understood when its external form and its internal arrangements are known. **Development** occupies a middle place between Morphology and Physiology; it is a morphological discipline in so far as it is concerned with the description of the parts of the developing organism; it is a physiological doctrine in so far as it studies the *activities* and *vital phenomena* during the course of development.

MATTER.—The entire visible world, including all organisms, consists of matter, *i.e.*, of substance which occupies space.

We distinguish *ponderable* matter which has weight, and *imponderable* matter which cannot be weighed in a balance. The latter is generally termed *ether*.

In ponderable materials, again, we distinguish their *form*, *i.e.*, the nature of their limiting surfaces; further, their *volume*, *i.e.*, the amount of space which they occupy; and lastly, their *aggregate condition*, *i.e.*, whether they are solid, fluid, or gaseous bodies.

Ether.—The ether fills the space of the universe, certainly as far as the most distant visible stars. This ether, notwithstanding its imponderability, possesses distinct mechanical properties; it is infinitely more attenuated than any known kind of gas, and behaves more like a solid body than a gas, resembling a gelatinous mass rather than the air. It participates in the luminous phenomena due to the vibrations of the atoms of the fixed stars, and hence it is the transmitter of light, which is conducted by means of its vibrations, with inconceivable rapidity (42,220 geographical miles per second) to our visual organs (*Tyndall*).

Imponderable matter (ether) and ponderable matter are not separated sharply from each other; rather does the ether penetrate into all the spaces existing between the smallest particles of ponderable matter.

Particles.—Supposing that ponderable matter were to be subdivided continuously into smaller and smaller portions, until we reach the last stage of division in which it is possible to recognise the *aggregate condition* of the matter operated upon, we should call the finely-divided portions of matter in this state *particles*. Particles of iron would still be recognised as *solid*, particles of water as *fluid*, particles of oxygen as *gaseous*.

Molecules.—Supposing, however, the process of division of the particles to be carried further still, we should at last reach a limit, beyond which, neither by mechanical nor by physical means, could any further division be effected. We should have arrived at the *molecules*. A molecule, therefore, is the smallest amount of matter which can still exist in a free condition, and which as a unit no longer exhibits the *aggregate condition*.

Atoms.—But even molecules are not the final units of matter, since every molecule consists of a group of smaller units, called *atoms*. An atom cannot exist by itself in a free condition, but the atoms unite with other similar or dissimilar atoms to form groups, which are called molecules. Atoms are incapable of further subdivision, hence their name. We assume that the atoms are invariably of the same size, and that they are solid. From a chemical point of view, the atom of

an elementary body (element) is the smallest amount of the element which can enter into a chemical combination. Just as ponderable matter consists in its ultimate parts of ponderable atoms, so does the ether consist of analogous small ether-atoms.

Ponderable and Imponderable Atoms.—The ponderable atoms within ponderable matter are arranged in a definite relation to the ether-atoms. The ponderable atoms mutually attract each other, and similarly they attract the imponderable ether-atoms; but the ether-atoms repel each other. Hence, in ponderable masses, ether-atoms surround every ponderable atom. These masses, in virtue of the attraction of the ponderable atoms, tend to come together, but only to the extent permitted by the surrounding ether-atoms. Thus the ponderable atoms can never come so close as not to leave interspaces. All matter must, therefore, be regarded as more or less loose and open in texture, a condition due to the interpenetrating ether-atoms, which resist the direct contact of the ponderable atoms.

Aggregate Condition of Atoms.—The relative arrangement of the molecules, *i.e.*, the smallest particles of matter which can be isolated in a free condition, determines the aggregate condition of the body.

Within a **solid** body, characterised by the permanence of its volume as well as by the independence of its form, the molecules are so arranged that they cannot readily be displaced from their relative positions.

Fluid bodies, although their volume is permanent, readily change their shape, and their molecules are in a condition of continual movement.

When this movement of the molecules takes so wide a range that the individual molecules fly apart, the body becomes **gaseous**, and as such is characterised by the instability of its form as well as by the changeableness of its volume.

Physics is the study of these molecules and their motions.

Forces.

1. Gravitation—Work done.—All phenomena appertain to matter. These phenomena are the appreciable expression of the forces inherent in matter. The forces themselves are not appreciable; they are the causes of the phenomena.

Gravitation.—The law of gravitation postulates that every particle of ponderable matter in the universe attracts every other particle with a certain force. This force is inversely as the square of the distance. Further, the attractive force is directly proportional to the amount of the attracting matter, without any reference to the quality of the body. We may estimate the intensity of gravitation by the extent of the movement which it communicates to a body allowed to fall, for one second, through a given distance, in a vacuous space. Such a body will fall *in vacuo* at the surface of the earth 9·809 metres per second. This fact has been arrived at experimentally.

Let us represent $g=9\cdot809$ metres, the final velocity of the freely falling body at the end of one second. The velocity, V , of the freely falling body is proportional to the time, t , so that

$$V=gt \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1);$$

i.e., at the end of the 1st sec., and $V=g$, $1=g=9\cdot809$ M—the distance traversed—

[illegible]

[illegible]

resting on the height; $\frac{m}{2}V_2$ is the kinetic energy corresponding to this potential energy (*Brücke*).

Potential energy may be transformed into mechanical energy under the most varied conditions; it may also be transferred from one body to another.

The movement of a pendulum is a striking example of the former. When the pendulum is at the highest point of its excursion, it must be regarded as absolutely at rest for an instant, and as endowed with potential energy, thus corresponding with the raised stone in the previous instance. During the swing of the pendulum this potential energy is changed into kinetic energy, which is greatest when the pendulum is moving most rapidly towards the vertical. As it rises again from the vertical position, it moves more slowly, and the kinetic energy is changed into potential energy, which once more reaches its maximum when the pendulum comes to rest at the utmost limit of its excursion. Were it not for the resistances continually opposed to its movements, such as the resistance of the air and friction, the movement of the pendulum, due to the alternating change of kinetic into potential energy and *vice versa*, would continue uninterruptedly, as with a mathematical pendulum. Suppose the swinging ball of the pendulum, when exactly in a vertical position, impinged upon a resting but movable sphere, the potential energy of the ball of the pendulum would be transferred directly to the sphere, provided that the elasticity of the ball of the pendulum and the sphere were complete; the pendulum would come to rest, while the sphere would move onward with an equal amount of kinetic energy, provided there were no resistance to its movement. This is an example of the transference of kinetic energy from one body to another. Lastly, suppose that a stretched watch-spring on uncoiling causes another spring to become coiled; and we have another example of the transference of kinetic energy from one body to another.

The following general statement is deducible from the foregoing examples:—If, in a system, the individual moving masses approach the final position of equilibrium, then in this system the sum of the *kinetic* energies increases; if, on the other hand, the particles move away from the final position of equilibrium, then the sum of the *potential* energies is increased at the expense of the kinetic energies, *i.e.*, the *kinetic* energies diminish (*Brücke*).

The pendulum, which, after swinging from the highest point of its excursion, approaches the vertical position, *i.e.*, the position of equilibrium of a passive pendulum, has in this position the largest amount of potential energy; as it again ascends to the highest point of its excursion on the other side, it again gradually receives the maximum of potential energy at the expense of the gradually diminishing movement, and therefore of the kinetic energy.

3. Heat.—*Its Relation to Potential and Kinetic Energy.*—If a lead weight be thrown from a high tower to the earth, and if it strike an unyielding substance, the movement of the mass of lead is not only arrested, but the kinetic energy (which to the eye appears to be lost) is transformed into a lively vibratory movement of the atoms. When the lead meets the earth, heat is produced. The amount of heat produced is proportional to the kinetic energy, which is transformed through the concussion. At the moment when the lead weight reaches the earth, the atoms are thrown into vibrations; they impinge upon each other; then rebound again from each other in consequence of their elasticity, which opposes their direct juxtaposition; they fly asunder to the maximum extent permitted by the attractive force of the ponderable atoms, and thus oscillate to and fro. All the atoms vibrate like a pendulum, until their movement is communicated to the ethereal atoms surrounding them on every side, *i.e.*, until the heat of the heated mass is “*radiated*.” *Heat is thus a vibratory movement of the atoms.*

As the amount of heat produced is proportional to the kinetic energy, which is transformed through the concussion, we must find an adequate measure for both forces.

Heat-Unit.—As a standard of measure of heat, we have the “heat-unit” or **calorie**. The “heat-unit” or calorie is the amount of energy required to raise the temperature of 1 gram of water 1° centigrade. The “heat-unit” corresponds to 425.5 gram-metres, *i.e.*, the same energy required to heat 1 gram of water 1° C. would raise a weight of 425.5 grams to the height of 1 metre; or, a weight of 425.5 grams, if allowed to fall from the height of 1 metre, would by its concussion produce as much heat as would raise the temperature of 1 gram of water 1° C. The “**mechanical equivalent**” of the heat-unit is, therefore, 425.5 gram-metres.

It is evident that from the collision of moving masses an immeasurable amount of heat can be produced. Let us apply what has already been said to the earth. Suppose the earth to be disturbed in its orbit, and suppose further that, owing to the attraction of the sun, it were to impinge on the latter (whereby, according to J. R. Mayer, its final velocity would be 85 geographical miles per second), the amount of heat produced by the collision would be equal to that produced by the combustion of a mass of pure charcoal more than 5000 times as heavy (*Julius Robert Mayer, Helmholtz*).

Thus, the heat of the sun itself can be produced by the collision of masses of cold matter. If the cold matter of the universe were thrown into space, and there left to the attraction of its particles, the collision of these particles would ultimately produce the light of the stars. At the present time, numerous cosmic bodies collide in space, while innumerable small meteors (94,000 to 188,000 billions of kilos. per minute) fall into the sun. The force of gravity is perhaps, in fact, the only source of all heat (*J. R. Mayer, Tyndall*).

We have a homely example of the transformation of kinetic energy into heat in the fact that a blacksmith may make a piece of iron red-hot by hammering it. Of the conversion of heat into kinetic energy we have an example in the hot watery vapour (steam) of the steam-engine raising the piston. An example of the conversion of potential energy into heat occurs in a metallic spring, when it uncoils and is so placed as to rub against a rough surface, producing heat by friction.

4. Chemical Affinity : Relation to heat.—Whilst gravity acts upon the particles of matter without reference to the composition of the body, there is another atomic force which acts between atoms of a chemically different nature; this is **chemical affinity**. This is the force in virtue of which the atoms of chemically different bodies unite to form a **chemical compound**. The force itself varies greatly between the atoms of different chemical bodies; thus we speak of strong chemical affinities and weak affinities. Just as we were able to estimate the potential energy of a body in motion from the amount of heat which was produced when it collided with an unyielding body, so we can measure the amount of heat which is formed when the atoms of chemically different bodies unite to form a chemical compound. As a rule, heat is formed when separate chemically-different atoms form a compound body. When, in virtue of chemical affinity, the atoms of 1 kilo. of hydrogen and 8 kilos. of oxygen unite to form the chemical compound *water*, an amount of heat is thereby evolved which is equal to that produced by a weight of 47,000 kilos. falling and colliding with the earth from a height of 1000 feet above the surface of the earth. If 1 gram of H be burned along with the requisite amount of O to form water, it yields 34,460 heat-units or calories; and 1 gram carbon burned to carbonic acid (carbon dioxide) yields 8080 heat-units.

Wherever, in chemical processes, strong chemical affinities are satisfied, heat is set free, i.e., chemical affinity is changed into heat. Chemical affinity is a form of potential energy obtaining between the most different atoms, which during chemical processes is changed into heat. Conversely, in those chemical processes where strong affinities are dissolved, and chemically-united atoms thereby pulled asunder, there must be a diminution of temperature, or, as it is said, *heat becomes latent*—that is, the energy of the heat which has become latent is changed into chemical energy, and this, after decomposition of the compound chemical body, is again represented by the chemical affinity between its isolated different atoms.

LAW OF THE CONSERVATION OF ENERGY.—Julius Robert Mayer and Helmholtz have established the important law that, in a system which does not receive any influence and impression from without, the sum of all the forces acting within it is always the same. *The various forms of energy can be transformed one into the other, so that kinetic energy may be transformed into potential energy and vice versa, but there is never any part of the energy lost.* The transformation takes place in such measure that, from a certain definite amount of one form of energy, a definite amount of another can be obtained.

The various forms of energy acting in organisms occur in the following modifications :—

1. **Molar motion** (ordinary movements), as in the movements of the whole body, of the limbs, or of the intestines, and even those observable microscopically in connection with cells.

2. **Movements of atoms as heat.**—We know, in connection with the vibration of atoms, that the number of vibrations in the unit of time determines whether the oscillations appear as heat, light, or chemically-active vibrations. Heat-vibrations have the smallest number, while chemically-active vibrations have the largest number, light-vibrations standing between the two. In the human body we only observe heat-vibrations, but some of the lower animals are capable of exhibiting the phenomena of light.

In the human organism the molar movements in the individual organs are constantly being transformed into heat, e.g., the kinetic energy in the organs of the circulation is transformed by friction into heat. The measure of this is the “**unit of work**” = 1 gram-metre, and the “**unit of heat**” = 425·5 gram-metres.

3. **Potential Energy.**—The organism contains many chemical compounds which are characterised by the great complexity of their constitution, by the imperfect saturation of their affinities, and hence by their great tendency to split up into simpler bodies.

The body can transform the potential energy into heat as well as into kinetic energy, the latter always in conjunction with the former, but the former always by itself alone. *The simplest measure of the potential energy is the amount of heat which can be obtained by complete combustion of the chemical compounds representing the potential energy.* The number of work-units can then be calculated from the amount of heat produced.

4. The phenomena of **electricity, magnetism, and diamagnetism** may be recognised in two directions, as movements of the smallest particles, which are

recognised in the glowing of a thin wire when it is traversed by strong electrical currents (against considerable resistance), and also as molar movement, as in the attraction or repulsion of the magnetic needle. Electrical phenomena are manifested in our bodies by muscle, nerve, and glands, but these phenomena are relatively small in amount when compared with the other forms of energy. It is not improbable that the electrical phenomena of our bodies become almost completely transformed into heat. As yet experiment has not determined with accuracy a "unit of electricity" directly comparable with the "heat-unit" and the "work-unit."

It is quite certain that within the organism one form of energy can be transformed into another form, and that a certain amount of one form will yield a definite amount of another form; further, that new energy never arises spontaneously, nor is energy already present ever destroyed, so that in the organism the law of the conservation of energy is continually in action.

ANIMALS AND PLANTS.—The animal body contains a quantity of chemically-potential energy stored up in its constituents. The total amount of the energy present in the human body might be measured by burning completely an entire human body in a *calorimeter*, and thereby determining how many heat-units are produced when it is reduced to ashes (see *Animal Heat*).

The chemical compounds containing the potential energy are characterised by the complicated relative position of their atoms, by a comparatively imperfect saturation of the affinities of their atoms, by the relatively small amount of oxygen which they contain, by their great tendency to decomposition, and the facility with which they undergo decomposition.

If a man were not supplied with food he would lose 50 grams of his body-weight every hour; the material part of his body, which contains the potential energy, is used up, oxygen is absorbed, and a continual process of combustion takes place; by the process of combustion simpler substances are formed from the more complex compounds, whereby potential is converted into kinetic energy. It is immaterial whether the combustion is rapid or slow; the same amount of the same chemical substances always produces the same amount of kinetic energy, *i.e.*, of heat.

A person, when fasting, experiences after a certain time the disagreeable feeling of exhaustion of his reserve of potential energy, hunger sets in, and he takes food. *All food for the animal kingdom is obtained, either directly or indirectly, from the vegetable kingdom.* Even carnivora, which eat the flesh of other animals, only eat organised matter which has been formed from vegetable food. The existence of the animal kingdom presupposes the existence of the vegetable kingdom.

All substances, therefore, necessary for the food of animals occur in vegetables. Besides **water** and the **inorganic constituents**, plants contain, amongst other organic compounds, the following *three chief representatives of food-stuffs*—**fats**, **carbohydrates**, and **proteids**.

All these contain stores of potential energy, in virtue of their complex chemical constitution.

The **fats** contain :— $\left\{ \begin{array}{l} \text{C}_n\text{H}_{2n-1}\text{O}(\text{OH}) = \text{fatty acids} \\ + \text{C}_3\text{H}_5(\text{OH})_3 = \text{glycerin} \end{array} \right\} \quad (\S\ 251).$

The **carbohydrates** contain :— $\text{C}_6\text{H}_{10}\text{O}_5 \quad . \quad . \quad (\S\ 252).$

The **proteids** contain per cent. :— $\left\{ \begin{array}{l} \text{C. } 51\cdot5\text{--}54\cdot5 \\ \text{H. } 6\cdot9\text{--}7\cdot3 \\ \text{N. } 15\cdot2\text{--}17\cdot0 \\ \text{O. } 20\cdot6\text{--}23\cdot5 \\ \text{S. } 0\cdot3\text{--}2\cdot0 \end{array} \right\} (\S\S 248 \text{ and } 249).$

A man who takes a certain amount of this food adds thereto **oxygen** from the air in the process of respiration. Combustion or oxidation then takes place, whereby chemically-potential energy is transformed into heat.

It is evident that the products of this combustion must be bodies of simpler constitution—bodies with less complex arrangement of their atoms, with the greatest possible saturation of the affinities of their atoms, of greater stability, partly rich in O, and possessing either no potential energy, or only very little. These bodies are **carbon dioxide**, CO_2 ; **water**, H_2O ; and as the chief representative of the nitrogenous excreta, **urea** ($\text{CO}(\text{NH}_2)_2$), which has still a small amount of potential energy, but which outside the body is readily converted into CO_2 and ammonia (NH_3).

The human body is an organism in which, by the phenomena of oxidation, the complex nutritive materials of the vegetable kingdom, which are highly charged with potential energy, are transformed into simple chemical bodies, whereby the potential energy is transformed into the equivalent amount of kinetic energy (heat, work, electrical phenomena).

But how do plants form these complex food-stuffs so rich in potential energy? It is plain that the potential energy of plants must be obtained from some other form of energy. This potential energy is supplied to plants by the **rays of the sun**, whose chemical light-rays are absorbed by plants. Without the rays of the sun there could be no plants. Plants absorb from the air and the soil CO_2 , H_2O , NH_3 , and N, of which carbon dioxide, water, and ammonia (from urea) are also produced by the excreta of animals. *Plants absorb the kinetic energy of light from the sun's rays and transform it into potential energy*, which is accumulated during the growth of the plant in its tissues, and in the food-stuffs produced in them during their growth. This formation of complex chemical compounds is accompanied by the simultaneous excretion of O.

Occasionally, kinetic energy, such as we universally meet with in animals, is liberated in plants. Many plants develop considerable quantities of heat in their flowers, *e.g.*, the arum tribe. We must also remember that during the formation of the solid parts of plants, when fluid juices are changed into solid masses, heat is set free. In plants, under certain circumstances, O is absorbed, and CO_2 is excreted, but these processes are so trivial as compared with the typical condition in the vegetable kingdom, that they may be regarded as of small moment.

Plants, therefore, are organisms which, by a reduction process, transform simple stable combinations into complex compounds, whereby potential solar energy is transformed into the chemically-potential energy of vegetable tissues. **Animals** are living beings, which by oxidation decompose or break up the complex grouping of atoms manufactured by plants, whereby potential is transformed into kinetic energy. Thus, there is a constant circulation of matter and a constant exchange of energy between plants and animals. All the energy of animals is derived from plants. All the energy of plants arises from the sun. Thus the sun is the cause, the original source of all energy in the organism, *i.e.*, of the whole of life.

As the formation of solar heat and solar light is explicable by the gravitation of masses, gravity is *perhaps* the original form of energy of all life.

We may thus represent the formation of kinetic energy in the animal body from the potential energy of plants. Let us suppose the atoms of the substances formed in organisms, as simple small bodies, balls, or blocks. As long as these lie in a single layer, or in a few layers, upon the surface, there is a stable arrangement, and they continue to remain at rest. If, however, an artificial tower be built of these blocks, so that an unstable erection is produced, and the same tower be afterwards knocked down, then for this purpose we require—(1) the motor power of the workman who lifts and carries the blocks; (2) a blow or other impulse from without applied to the unstable structure—when the atoms will fall together, and as they fall collide with each other and produce heat. Thus, the energy employed by the workman is again transformed into the last-named form of energy.

In plants the complex unstable building of the groups of atoms is carried on, the constructor being the sun. In animals, which eat plants, the complex groups of the atoms are tumbled down, with the liberation of kinetic energy.

Vital Energy and Life.—The forces which act in organisms, in plants, and animals are exactly the same as are recognisable as acting in dead matter. A so-called “vital force,” as a special force of a peculiar kind, causing and governing the vital phenomena of living beings, does not exist. The forces of all matter, of organised as well as unorganised, exist in connection with their smallest particles or atoms. As, however, the smallest particles of organised matter are, for the most part, arranged in a very complicated way, compared with the much simpler composition of inorganic bodies, so the forces of the organism connected with the smallest particles yield more complicated phenomena and combinations, whereby it is excessively difficult to ascribe the vital phenomena in organisms to the simple fundamental laws of physics and chemistry.

The Exchange of Material, or Metabolism (“*Stoffwechsel*”) as a Sign of Life.—Nevertheless, there appears to be a special exchange of matter and energy peculiar to living beings. This consists in the capacity of organisms to assimilate the matter of their surroundings, and to work it up into their own constitution, so that it forms for a time an integral part of the living being, to be given off again. The whole series of phenomena is called **metabolism** or “*Stoffwechsel*,” which consists in the introduction, assimilation, integration, and excretion of matter.

We have already shown that the metabolism of plants and that of animals are quite different. The processes, as already described, actually occur in the typical higher plants and animals.

But there is a large group of organisms which, throughout their entire organisation, exhibit so low a degree of development, that by some observers they are considered as undifferentiated “ground-forms.” They are regarded as neither plants nor animals, and are the most simple forms of animated matter. Haeckel has called these organisms **Protistæ**, as being the original and primitive forms.

We must assume that, corresponding with their simpler vital conditions, their metabolism is also simpler, but on this point we still require further observations and experiments.

Physiology of the Blood.

[THE blood is aptly described by Claude Bernard as an **internal medium** which acts as a “go-between” or **medium of exchange** for the outer world and the tissues. Into it are poured those substances which have been subjected to the action of the digestive fluids, and in the lungs or other respiratory organs it receives oxygen. It thus contains **new substances**, but in its passage through the tissues it gives up some of these new substances, and receives in exchange certain **waste products** which have to be got rid of. Its composition is thus highly complex. Besides carrying the *new* nutrient fluids to the tissues, it is also the great **oxygen-carrier**, as well as the medium by which some of the waste products, *e.g.*, CO_2 , urea, are removed *from* the tissues, and brought to the organs, *e.g.*, the lungs, kidneys, skin, which eliminate them from the body. It is at once a great pabulum-supplying medium and a channel for getting rid of useless materials. As the composition of the organs through which the blood flows varies, it is evident that its composition must vary in different parts of the circulatory system; and it also varies in the same individual under different conditions. Still with slight variations, there are certain general physical, histological, and chemical properties which characterise blood as a whole.]

1. PHYSICAL PROPERTIES.—(1) **Colour.**—The colour of blood varies from a bright scarlet-red in the arteries to a deep, dark, bluish-red in the veins. Oxygen (and, therefore, the air) makes the blood bright red; want of oxygen makes it dark. Blood free from oxygen (and also venous blood) is *dichroic*—*i.e.*, by reflected light it appears dark red, while by transmitted light it is green. [Arterial blood is *monochroic*.]

In thin layers blood is **opaque**, as is easily shown by shaking blood so as to form bubbles, or by allowing blood to fall upon a plate with a pattern on it, and pouring it off again. [Printed matter cannot be read through a thin layer of blood spread on a glass slide.] Blood behaves, therefore, like an “opaque colour,” as its colouring matter is suspended in the form of fine particles—the blood-corpuscles.

Hence, it is possible to separate the colouring-matter from the fluid part of the blood by filtration. This is accomplished by mixing the blood with fluids which render the blood-corpuscles sticky or rough. If mammalian blood be treated with one-seventh of its volume of solution of sodic sulphate, or if frog's blood be mixed with a 2 per cent. solution of sugar (*Joh. Müller*) and filtered, the shrivelled corpuscles, now robbed of part of their water, remain upon the filter.

(2) **Reaction.**—The reaction is alkaline, owing to the presence of disodic phosphate, Na_2HPO_4 , and bicarbonate of soda. After blood is shed, its alkalinity rapidly diminishes, and this occurs more rapidly the greater the alkalinity of the blood. This is due to the formation of an acid, in which, perhaps, the coloured corpuscles take part, owing to the decomposition of their colouring matter. A high

temperature and the addition of an alkali favour the formation of the acid (*N. Zuntz*).

The alkaline reaction of blood is **diminished**: (a) by great muscular exertion, owing to the formation of a large amount of acid in the muscles; (b) during coagulation; (c) in old blood, or blood dissolved by water from old blood-stains, such blood being usually acid; fresh cruer has a stronger alkaline reaction than serum; (d) after the prolonged use of soda the alkalinity is increased, after the use of acids it is decreased. In women and children the alkalescence is less than in man, and it is less in lying-in women than in pregnant women (*Peiper*).

Methods.—Owing to the colour of the blood we cannot employ ordinary litmus paper to test its reaction. One of the following methods may be used:—(1) Moisten a strip of glazed red litmus paper with solution of common salt, and allow a drop of blood to fall on the paper; then rapidly wipe it off before its colouring matter has time to penetrate and tinge the paper (*Zuntz*). (2) *Liebreich* used thin plates of plaster-of-Paris of a perfectly neutral reaction. These are dried, and afterwards moistened with a neutral solution of litmus. When a drop of blood is placed upon the porous plate, the fluid part of the blood passes into it, the corpuscles are then washed off with water, and the altered colour of the litmus-stained slab is apparent. [(3) *Schäfer* uses dry faintly-reddened glazed litmus paper, and on it is placed a drop of blood, which is wiped off after a few seconds. The place where the blood rested is indicated by a blue patch upon a red or violet ground.]

Estimation of the Alkalinity.—A very dilute solution of tartaric acid (1 cubic centimetre combines with 3.1 milligrams of soda, *i.e.*, 1 litre of water contains 7.5 grams of crystallised tartaric acid) is added to blood until a blue litmus paper is turned red (by *Zuntz*'s method). 100 grams of rabbit's blood have an alkalinity corresponding to 150 milligrams of soda; the blood of carnivora to about 180 milligrams (*Lassar*), while 100 c.c. of normal human blood have an alkalinity equal to 260–300 milligrams of soda (*v. Jaksch*).

The following method can be used with a few drops of blood:—To neutralise the blood, tartaric acid in the above concentration is used. Prepare the following mixtures by mixing the tartaric acid solution with a concentrated neutral solution of sodic sulphate, and then adding sodic sulphate until the mixture is completely saturated. I., 10 parts of solution of tartaric acid to 100 parts of concentrated sodic sulphate solution; II., 20 parts tartaric acid solution to 90 sodic sulphate solution; III. contains these substances in the proportion of 30 to 80; IV., 40 to 70; V., 50 to 60; VI., 60 to 50; VII., 70 to 40; VIII., 80 to 30; IX., 90 to 20; and X., 100 to 10. Excess of sodic sulphate is present in all the flasks.

A known volume of the blood to be investigated is mixed with an equal volume of each of the mixtures, in a small tube, which is made by drawing out a glass tube 1 millimetre in diameter to a fine point. To calibrate this tube, suck up water, say, to the height of 8 mm., make a mark on the tube with a fine file, then suck up the water until its lower level corresponds with the mark. Again mark the upper limit of the water. To test the blood, suck a drop of the mixture I. up to the level of the first mark on the glass pipette, and, after wiping its point, suck up an equal quantity of blood. Again clean the point of the pipette, and blow its contents into a watch-glass; then mix, and test the reaction with sensitive violet-coloured litmus paper. Proceed in the same way with the several mixtures, II. to X., until the alkaline reaction disappears or the acid appears. The narrow strips of litmus paper are dipped into each of the mixtures, the corpuscles remain in the wetted part of the paper, while the fluid permeates further and shows the reaction. As a rule, the degree of alkalinity in human blood of adults corresponds to VI., and in children to IV. Human blood can be sucked directly from a small wound made by a needle, either by attaching an elastic tube or a small hypodermic syringe to the pipette (*Landois*).

Pathological.—The alkalinity is **increased** during persistent vomiting, and **decreased** in pronounced anæmia, cachexia, uræmia, rheumatism, high fever, diabetes, in poisoning with CO, degenerations of the liver, and cholera. [Immediately before death by cholera it may be acid (*Cantani*).]

(3) **Odour.**—Blood emits a peculiar odour, the *halitus sanguinis*, which differs in animals and man.

It depends upon the presence of volatile fatty acids. If concentrated sulphuric acid [1½ vols.] be added to blood, whereby the volatile fatty acids are set free from their combinations with alkalies, the characteristic odour, somewhat similar to that of butyric acid, becomes much more perceptible.

(4) **Taste.**—Blood has a saline taste, depending upon the salts dissolved in the fluid of the blood.

(5) **Specific Gravity.**—The specific gravity is 1056–1059 in man, 1051–1055 in woman; in children less. The specific gravity of the blood-corpuscles is 1105, that of the plasma 1027. Hence the corpuscles tend to sink.

Clinical Method.—A thin glass tube is drawn out till it is of small calibre, and then bent at a right angle, and closed above with a caoutchouc cap, thus forming a small pipette. With this pipette, suck up a drop of freshly-drawn blood obtained by pricking the finger. The fine capillary-tube is at once immersed in a solution of sodic sulphate, and a drop of the blood expressed into the saline solution. It is necessary to prepare several solutions of sodic sulphate with specific gravities varying from 1050–1070. The solution in which the corpuscles remain suspended indicates the specific gravity of the blood (*Roy, Landois*).

The drinking of water and hunger diminish the specific gravity temporarily, while thirst and the digestion of dry food raise it. If blood be passed through an organ artificially, its specific gravity rises in consequence of the absorption of dissolved matters and the giving off of water. It falls after hæmorrhage, and is diminished in badly-nourished individuals. [By working with solutions of glycerine, Jones finds that it is the highest at birth, and at a minimum between the second week and the second year; it rises gradually until the 35th–45th year. It is usually higher in the male than the female, is diminished by pregnancy, the ingestion of solid or liquid food, and gentle exercise.]

[(6) **Temperature.**—Blood is viscid, and its temperature varies from 36.5° C. (97.7° F.) to 37.8° (100° F.). The warmest blood in the body is that of the hepatic vein (§ 210).]

2. MICROSCOPIC EXAMINATION.—[Blood, when examined by the microscope, is seen to consist of an enormous number of **corpuscles**—coloured and colourless—floating in a transparent fluid, the **plasma**, or **liquor sanguinis**, together with the blood-plates or platelets.]

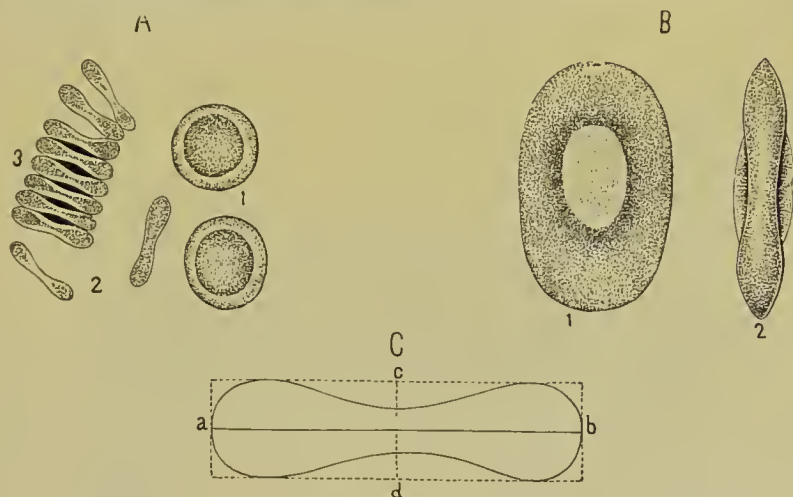


Fig. 1.

A, human coloured blood-corpuscles—1, on the flat; 2, on edge; 3, rouleau of coloured corpuscles. B, amphibian coloured blood-corpuscles—1, on the flat; 2, on edge. C, ideal transverse section of a human coloured blood-corpuscle magnified 5000 times linear—*ab*, diameter; *cd*, thickness.

I. Human Red Blood-Corpuscles.—(a) **Form.**—They are circular, coin-shaped, homogeneous discs, with saucer-like depressions on both surfaces, and with rounded margins; in other words, they are bi-concave, circular non-nucleated discs (figs. 1, A; 5).

(b) **Size.**—The diameter (*ab*) is 7.7μ ,¹ (6.7 – 9.3μ) the greatest thickness (*cd*) 1.9μ (fig. 1, C), [i.e., it is $\frac{1}{3500}$ to $\frac{1}{3200}$ of an inch in diameter, and about one-fourth of that in thickness].

They are slightly diminished in size by septic fever, inanition, morphia, increased bodily temperature, and CO_2 ; and increased by O_2 , watery condition of the blood, cold, consumption of alcohol, quinine, and hydrocyanic acid. Compare § 10, 2.

If the total amount of blood in a man be taken at 4400 cubic centimetres, the corpuscles,

¹ The Greek letter μ represents one-thousandth of a millimetre ($\mu = 0.001$ mm.), and is the sign of a *micro-millimetre*, or a *micron*.

therein contained have a surface of 2816 square metres, which is equal to a square surface with a side of 80 paces; 176 cubic centimetres of blood pass through the lungs in a second, and the blood-corpuscles in this amount of blood have a superficies of 81 square metres, equal to a square surface with a side of 13 paces (*Welcker*).

(c) The weight of a blood-corpuscle is 0.00008 milligram.

[(d) **Colour and Transparency.**—Each corpuscle is of a light straw-yellow colour; but when seen *en masse* the corpuscles are red. They are fairly transparent; thus the outline of one corpuscle can be distinctly seen through another corpuscle lying above it.]

(e) The number exceeds 5,000,000 per cubic millimetre in the male, and 4,500,000 in the female; so that, in 10 lbs. of blood, there are 25 billions of corpuscles. The number is in inverse ratio to the amount of plasma; hence, the number must vary with the state of contraction of the blood-vessels, the pressure, diffusion currents, and other conditions.

The number of red corpuscles is **increased**; in venous blood (especially in the small cutaneous veins), after the use of solid food, after much sweating, and the excretion of much water by the bowel and kidneys; during inanition, because the blood-plasma undergoes decomposition sooner than the blood-corpuscles themselves; in the blood of the newly-born child, especially

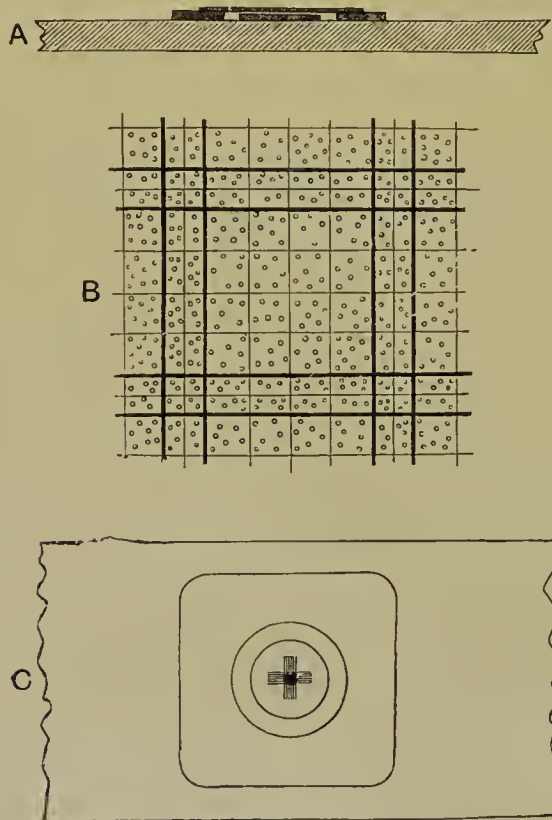


Fig. 2.

Apparatus of Abbe and Zeiss for counting the corpuscles. A, in section; C, surface view without cover-glass; B, microscopic appearance with the blood-corpuscles.

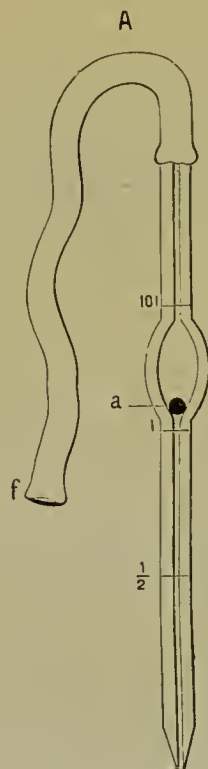


Fig. 3.

The *Mélangeur* pipette or mixer.

when the umbilical cord is long in being tied (§ 40), from the 4th day onward the number is diminished; in persons of robust constitution, and in those who live in the country. The number is diminished, during pregnancy, and after copious draughts of water. In the earlier period of fetal life the number is only $\frac{1}{2}$ –1 million in 1 cubic millimetre. (For the pathological conditions see § 10.)

Methods of Counting the Blood-Corpuscles.—The pointed end of a glass pipette (fig. 3), the mixer, is dipped into the blood, and by sucking the elastic tube *f*, blood is drawn into the tube until it reaches the mark $\frac{1}{2}$, on the stem of the pipette, or until the mark 1 is reached. The carefully-cleaned point of the pipette is dipped into the artificial serum, and this is sucked into the pipette until it reaches the mark, 101. The artificial serum consists of 1 vol. of solution of gum arabic (sp. gr. 1020) and 3 vols. of a solution of equal parts of sodic sulphate and sodic chloride (sp. gr. 1020). The process of mixing the two fluids is aided by the presence of a little glass ball (*a*) in the bulb of the pipette. If blood is sucked up to the mark $\frac{1}{2}$, the strength of the mixture is 1 : 200; if to the mark 1, it is 1 : 100; a small drop of the mixture is allowed to run into the counting-chamber of Abbe and Zeiss (fig. 2). The first portions are not used, in order to obtain a uniform sample from the bulb of the pipette. This chamber consists of a glass receptacle 0.1 mm. deep, with its base divided into squares, and cemented to a glass slide, the whole being covered with a thin covering-glass. The space over each square = $\frac{1}{1000}$ cubic millimetre. Count, with the aid of a microscope, the number of blood-corpuscles in each square, and the number found, multiplied by 4000, will give the number of blood-corpuscles in 1 c.mm. This number, again, must be multiplied by 100 or 200, according as the blood was diluted 100 or 200 times. To ensure greater accuracy, it is well to count the number in several squares, and to take the mean of these.

[Gowers' method.]—“The Hæmacytometer (fig. 4) consists of—(1) a small pipette, which, when filled to the mark on its stem, holds exactly 995 cubic millimetres. It is furnished with an india-rubber tube and mouthpiece to facilitate filling and emptying. (2) A capillary tube

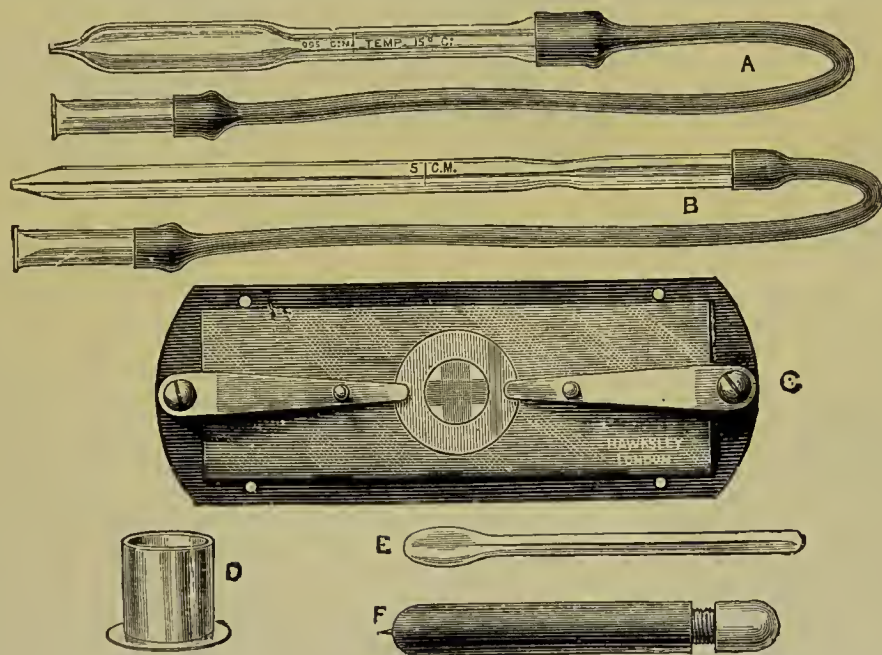


Fig. 4.

Gowers' apparatus. A, pipette for measuring the diluting solution; B, capillary tube for measuring the blood; C, cell with divisions on the floor, mounted on a slide; D, vessel in which the dilution is made; E, glass stirrer; F, guarded spear-pointed needle.

marked to contain exactly 5 cubic millimetres, with india-rubber tube for filling, &c. (3) A small glass jar in which the dilution is made. (4) A glass stirrer for mixing the blood and solution in the glass jar. (5) A brass stage plate, carrying a glass slip, on which is a cell, $\frac{1}{10}$ of a millimetre deep. The bottom of this is divided into $\frac{1}{10}$ millimetre squares. Upon the top of the cell rests the cover-glass, which is kept in its place by the pressure of two springs proceeding from the ends of the stage plate." The diluting solution used is a solution of sodic sulphate in distilled water, sp. gr. 1025, or the following:—sodic sulphate, 104 grains; acetic acid, 1 drachm; distilled water, 4 oz.

"995 cubic millimetres of the solution are placed in the mixing jar; 5 cubic millimetres of blood are drawn into the capillary tube from the puncture in the finger, and then blown into the solution. The two fluids are well mixed by rotating the stirrer between the thumb and finger, and a small drop of this dilution is placed in the centre of the cell, the covering-glass gently put upon the cell, and secured by the two springs, and the plate placed upon the stage

of the microscope. The lens is then focussed for the squares. In a few minutes the corpuscles have sunk to the bottom of the cell, and are seen at rest on the squares. The number in ten squares is then counted, and this, multiplied by 10,000, gives the number in a cubic millimetre of blood."

To estimate the colourless corpuscles only, mix the blood with 10 parts of 0.5 per cent. solution of acetic acid, which destroys all the red corpuscles (*Thoma*).

3. HISTOLOGY OF THE HUMAN RED BLOOD-CORPUSCLES AND THE EFFECT OF REAGENTS.—

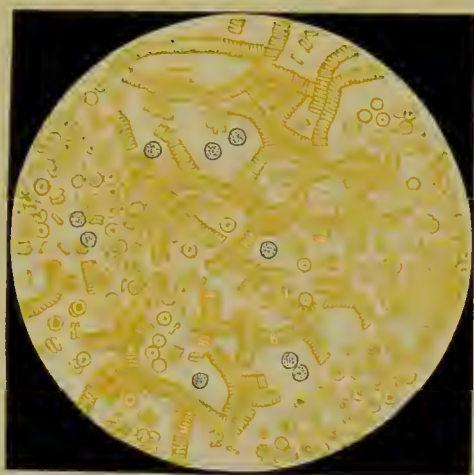


Fig. 5.

Drop of human blood showing some of the red corpuscles in rouleaux.

are bi-concave circular discs of a yellow colour with a slight tinge of green; they seem to be devoid of an envelope, are certainly non-nucleated, and appear to be homogeneous throughout (fig. 5). Each corpuscle consists (1) of a framework, an exceedingly pale, transparent, soft protoplasm—the **stroma**; and (2) of the **pigment or hæmoglobin**, which impregnates the stroma, much as fluid passes into and is retained in the interstices of a bath-sponge.

(A) **Effects of reagents on their Vital Phenomena.**—The blood-corpuscles present in shed blood—or even in defibrinated blood, when it is reintroduced into the circulation—retain their vitality and functions undiminished. **Heat** acts powerfully on their vitality, for if blood be heated to 52°C ., the vitality of the red corpuscles is destroyed. Mammalian

blood may be kept for four or five days in a vessel under iced water, and still retain its functions; but if it be kept longer, and reintroduced into the circulation, the corpuscles rapidly break up—a proof that they have lost their vitality. The red corpuscles in freshly shed blood sometimes exhibit a peculiar mulberry-like appearance (figs. 6, 7, *g*, *h*). [This is called **crenation** of the coloured corpuscles. It occurs in cases of poisoning with Calabar bean; and also by the addition of a 2 per cent. solution of common salt.] The blood of many persons

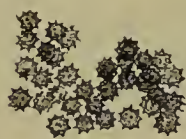


Fig. 6.

Crenation of human red blood-corpuscles. $\times 300$. crenates spontaneously—a condition ascribed to an active contraction of the stroma, but it is doubtful if this is the cause. The red corpuscles of the embryo-chick undergo active contraction.

(B) **On their External Characters.**—(*a*) The **colour** is changed by many gases. O makes blood scarlet, want of O renders it dark bluish-red, CO makes it cherry-red, NO violet-red. There is no difference between the shape of the corpuscles in arterial and venous blood. All reagents (*e.g.*, a concentrated solution of sodic sulphate), which cause great shrinking of the coloured corpuscles, produce a very bright scarlet or brick-red colour. The red colour so produced is quite different from the scarlet-red of arterial blood. Reagents which render blood-corpuscles globular darken the blood, *e.g.*, water.

[The contrast is very striking, if we compare blood to which a 10 per cent. solution of common salt has been added with blood to which water has been added. With reflected light the one is bright red, and the other a very dark deep crimson, almost black.]

(*b*) **Formation of Rouleaux.**—A very common phenomenon in shed blood is the tendency of the corpuscles to run into rouleaux (figs. 1, A 3; 5).

Conditions that increase the coagulability of the blood favour this phenomenon, which is ascribed by Dogiel to the attraction of the discs and the formation of a sticky substance. [The cause of the formation of rouleaux is by no means clear. The corpuscles may be detached from each other by gently touching the cover-glass, but the rouleaux may re-form. Lister suggested

that the surfaces of the corpuscles were so altered that they became adhesive. Norris made experiments with corks weighted with tacks or pins, so as to produce partial submersion of the cork discs. These discs rapidly cohere, owing to capillarity, and form rouleaux. If the discs be completely submerged they remain apart, as occurs with unaltered blood-corpuscles within the blood-vessels. If, however, the corpuscles be dipped in petroleum, and then placed in water, rouleaux are formed.] If reagents which cause the corpuscles to swell up be added to the blood, the corpuscles become globular and the rouleaux break up. According to E. Weber and Suchard, the uniting medium is not fibrin (although it may sometimes assume a fibrous form), but belongs to the peripheral layer of the corpuscles.

(c) **Changes of Form.**—The discharge of a Leyden jar causes the corpuscles to

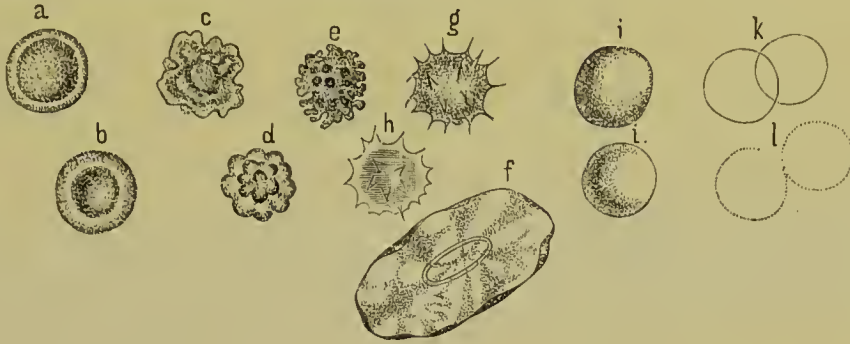


Fig. 7.

Red blood-corpuscles. *a, b*, normal human red corpuscles, the central depression more or less in focus; *c, d, e*, mulberry, and *g, h*, crenated forms; *k*, pale corpuscles decolorised by water; *l*, stroma; *f*, frog's blood-corpuscle acted on by a strong saline solution.

crenate, so that their surfaces are beset with coarse or fine projections (fig. 7, *c, d, e, g, h*); it also causes the corpuscles to assume a spheroidal form (*i, j*), and they become smaller than normal. The corpuscles so altered are sticky, and run together like drops of oil, forming larger spheres. The prolonged action of the electrical spark causes the hæmoglobin to separate from the stroma (*k*), whereby the fluid part of the blood is reddened, while the stroma is recognisable only as a faint shadow (*l*). Similar forms are to be found in decomposing blood, as well as after the action of many other reagents. **Heat.**—When blood is heated, on a warm stage, to 52° C. the corpuscles exhibit remarkable changes. Some of them become spherical, others biscuit-shaped; some are perforated, while in others small portions become detached and swim about in the surrounding fluid, a proof that heat destroys the histological individuality of the corpuscles (fig. 8). If the heat be continued, the corpuscles are dissolved (§ 10, 3).

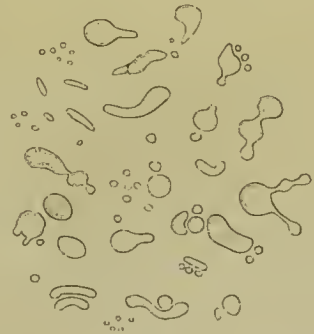


Fig. 8.

Effect of heat on human coloured blood-corpuscles. (*Stirling*)
× 400.

The addition of a concentrated solution of urea to blood acts like heat on the blood-corpuscles. If strong pressure be exerted upon a microscopic preparation, the blood-corpuscles may break in pieces. The latter process is called **hæmocytolysis**, in contradistinction to that of solution of the corpuscles or **hæmocytolysis**.

If a finger moistened with blood be rapidly drawn across a warm slip of glass, so that the fluid dries rapidly, the corpuscles exhibit very remarkable shapes, showing their great ductility and softness.

[Water renders the red corpuscles spherical, although some of them do not become quite so, as there remains a slight depression or umbilicus on one side of the corpuscle. Gradually they are decolorised, and only the stroma—the outline of which is difficult to see—remains in the field of the microscope (fig. 7, *k, l*). The water passes into the corpuscles by osmosis, and dissolves out the hæmoglobin.]

Saline solutions in certain concentrations (2-3 per cent.) make them crenated (fig. 6).

[Acetic acid renders them clear and transparent, and dissolves out the hæmoglobin. See p. 9 for other acids. Alkalies in very dilute solutions make them spherical, and ultimately completely dissolve them.]

[Hamburger has studied the action of saline solutions of various strengths. The strength of a solution in which the corpuscles remain unaltered he calls the isotonic or neutral point (0.64 per cent. for NaCl, and 5.59 per cent. of sugar).]

Cytozoon—Gaule's Experiment.—A few drops of freshly-shed frog's blood are mixed with 5 c.c. of 0.6 per cent. solution of common salt, and the mixture defibrinated by shaking it along with a few c.c. of mercury. A drop of the defibrinated blood is examined on a hot stage (30°-32° C.) under a microscope, when a protoplasmic mass, the so-called "*Wärmehen*," escapes with a lively movement from many corpuscles, and ultimately dissolves. Similar "cytozoa" were discovered by Gaule in the epithelium of the cornea, of the stomach and intestine, in connective-tissue, in most of the large glands, and in the retina (frog, triton). In mammals also he found similar but smaller structures. Most probably these structures are parasitic in their nature, as suggested by Ray Lankester, who called the parasite *Drepanidium ranarum*.

[**Staining Reagents.**—Such reagents as magenta, picro-carmin, carmin, and many of the aniline dyes, stain the nucleus deeply when such is present, and although they must traverse the hæmoglobin to reach the nucleus, the hæmoglobin itself is not stained. When no nucleus is present, therefore, the corpuscles are not stained. Magenta causes one or more small spots or maculæ to appear on the edge of the corpuscles (fig. 9, a). What its significance is is entirely unknown. Normal

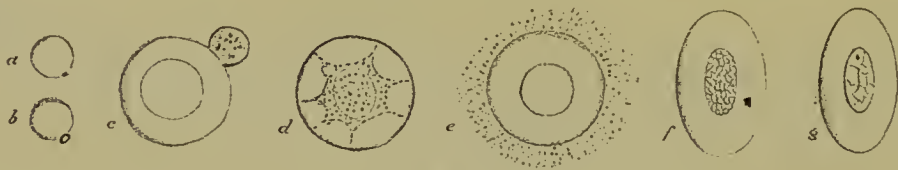


Fig. 9.

a, b, human red blood-corpuscles; a, acted on by magenta; b, by tannic acid. The others are amphibian red blood-corpuscles; c, d, e, effect of tannic acid; f, of dilute acetic acid; g, of dilute alcohol; h, of boracic acid (*Stirling*).

saline solution (0.6 per cent. NaCl), tinged with methyl violet, is a good staining and preservative agent. Red corpuscles become green when they are treated with indigo-carmin and borax, and then with oxalic acid. By means of this reaction Bayerl discovered the formation of red corpuscles in ossifying cartilage (p. 12).

[**Agitation with Mercury.**—If ox blood be shaken up with mercury for 7 or 8 hours, the corpuscles completely disappear, no trace of stroma or corpuscles being found in the fluid (*Meltzer and Welch*). The addition of pyrogallie acid (20 per cent.), potassic chlorate (6 per cent.), and silver nitrate (3 per cent.), completely prevents dissolution of the corpuscles, even though the shaking be kept up for fourteen days.]

If blood be mixed with concentrated gum solution, and if concentrated salt solution be added to it under the microscope, the corpuscles assume elongated forms. Similar forms are obtained by mixing blood with an equal volume of gelatine at 36° C., allowing it to cool, and then making sections of the coagulated mass. The corpuscles may be broken up by pressing firmly on the cover-glass. In all these experiments no trace of an envelope around the corpuscles is observed.

4. CONSERVATION OF THE CORPUSCLES.—The blood-corpuscles retain their form in the following fluid:—

Pacini's Fluid:—

Mercuric chloride,	2 grams.
Sodic chloride,	4 „
Glycerine,	26 c.c.
Water,	226 „

Hayem's Fluid:—

Mercuric chloride,	0.5 grams.
Sodic sulphate,	5 „
Sodic chloride,	1 „
Water,	200 c.c.

Before using it dilute it with 2 parts water.

1 per cent. osmic acid, 0.6 per cent. NaCl, and other fluids, have also been recommended for this purpose. In order to investigate fresh human blood without contact with air, place a drop of Hayem's or Pacini's fluid on the skin and prick the skin through the drop of fluid. The blood runs into and mixes with the fluid without coming into contact with the air. If a drop

of blood be rapidly dried in a thin layer on a slide, the corpuscles retain their form and colour; and if the process be done with sufficient rapidity, even the blood-platelets are retained.

In investigating blood with the microscope for forensic purposes, it is necessary to have a solvent for the blood when it occurs as stains on a garment or instrument. Dried stains are dissolved by a concentrated, or a 30 per cent., solution of caustic potash, or with one of the preserving fluids. If the stain be softened with concentrated tartaric acid, the colourless corpuscles are specially distinct (*Struve*). Nevertheless, corpuscles are often *not* found in such stains. If the corpuscles have become very pale, their colour may be improved by adding a solution of iodide of potassium, a saturated solution of picric acid, 20 per cent. pyrogallie acid, or 3 per cent. solution of silver nitrate.

5. STROMA—LAKE-COLOURED BLOOD.—Many reagents cause the hæmoglobin to separate from the stroma. The hæmoglobin dissolves in the serum; the blood becomes dark red and transparent, as it contains its colouring matter in solution, and hence it is called “lake-coloured” (*Rollett*). The aggregate condition of the hæmoglobin is not altered when the corpuscles are dissolved—it only changes its place, leaving the stroma and passing into the serum. Hence, the temperature of the blood is not lowered thereby.

Methods.—To obtain a large quantity of the stroma for chemical purposes add 10 vols. of a solution of common salt (1 vol. concentrated solution and 15 to 20 vols. of water) to 1 vol. of defibrinated blood, when the stromata are thrown down as a whitish precipitate.

For **microscopical purposes** mix blood with an equal volume of a concentrated solution of sodic sulphate, and cautiously add a 1 per cent. solution of tartaric acid.

The following reagents cause a separation of the stroma from the hæmoglobin, and thus make blood transparent :—

(a) **Physical Agents.**—1. Heating the blood to 60° C. (*Schultze*); the temperature, however, varies for the blood of different animals. 2. Repeated freezing and thawing of the blood (*Rollett*). 3. Sparks from an electrical machine (but not after the addition of salts to the blood) (*Rollett*); the constant and induced currents (*Neumann*).

(b) **Chemically active Substances produced within the Body.**—

4. Bile (*Hünefeld*) or bile salts (*Plattner, v. Dusch*).

5. Serum of other species of animals (*Landois*); thus dog's serum and frog's serum dissolve the blood-corpuscles of the rabbit in a few minutes. 6. The addition of lake-coloured blood of many species of animals (*Landois*).

(c) **Other Chemical Reagents.**—7. Water. 8. The vapour of

chloroform (*Böttcher*); ether (*v. Wittich*); amyls, small quantities of alcohol (*Rollett*); thymol (*Marchand*); nitrobenzol, paraldehyde, ethylic ether, acetone, petroleum ether, &c. (*L. Lewin*). 9. Antimoniuretted hydrogen, arseniuretted

hydrogen; carbon bisulphide; boracic acid (2 per cent.), added to the amphibian blood, causes the red mass (which also encloses the nucleus when such is present), the so-called zooid, to separate from the œcoid (fig. 9, d). The zooid may shrink from the periphery of the corpuscle, or it may pass out of the corpuscle altogether (*Brücke*); *Brücke* regards the stroma in a certain sense as a house, in which the remainder of the substance of the corpuscle, the chief part endowed with vital phenomena, lives. 11. Strong solutions of acids dissolve the corpuscles; more dilute solutions cause precipitates in the hæmoglobin. This is easily seen with carbolic acid (*Hüls and Landois, Stirling and Rannie*). 12. Alkalies of moderate strength cause sudden solution. A 10 per cent. solution of potash placed at the edge of a cover-glass, shows the process of solution going on under the microscope. At first the corpuscles become globular, and so appear smaller, but afterwards they burst like soap-bubbles. 13. Such salt solutions, which in plants cause a separation of the protoplasm from the cell-membrane (plasmolysis), make ox-blood lake-coloured. [14. NH_4Cl injected into the blood causes vacuolation of the red corpuscles (*Bobritzky*). 15. Sodic salicylate, benzoate, and colehiacin dissolve the red corpuscles (*N. Paton*).]

[**Tannic Acid.**—A freshly prepared solution of tannic acid has a remarkable effect on the coloured blood-corpuscles of man and animals—causing a separation of the hæmoglobin from the stroma (*W. Roberts*). The usual effect is to produce one or more granular buds of hæmoglobin on the side of the corpuscles (fig. 9, b, c); more rarely the hæmoglobin collects around the nucleus, if such be present (fig. 9, d), or is extruded, as shown in fig. 9, e.]

[**Ammonium or Potassium Sulphocyanide** removes the hæmoglobin, and reveals a reticular structure—*intra-nuclear* plexus of fibrils (*Stirling and Rannie*).]

[**Syrup** causes some of the red corpuscles to become twisted, and to exhibit redder patches in them (fig. 10).]



Fig. 10.

Red blood-corpuscles of the frog acted on by syrup (*Stirling*).

The **Amount of Gases** in the blood exercises an important influence on their solubility. The corpuscles of venous blood, which contains much CO_2 , are more easily dissolved than those of arterial blood; while between both stands blood containing CO . When the gases are completely removed from the blood, it becomes lake-coloured.

Salts increase the resistance of the corpuscles to physical means of solution, while they facilitate the action of chemical solvents.

If certain salts be added in substance to blood, they make blood lake-coloured; potassic sulphocyanide, sodic chloride, &c. (*Kowalewsky*).

Resistance to Solvents.—The red blood-corpuscles offer a certain degree of resistance to the action of solvents.

Method.—Mix a small drop of blood with an equal volume of a 3 per cent. solution of sodic chloride, and then add distilled water until all the coloured corpuscles are dissolved. Fill the mixer (fig. 3) up to the mark 1 with blood obtained by pricking the finger, and blow this blood into an equal volume of a 3 per cent. solution of NaCl previously placed in a hollow in a glass slide. Mix the fluids, and the corpuscles will remain undissolved. By means of the pipette add distilled water, and go on doing so until all the corpuscles are dissolved; which is ascertained with the microscope. In normal blood, solution of the corpuscles occurs after 30 volumes of distilled water have been added to the blood (*Landois*).

There are some individuals whose blood is more soluble than that of others; their corpuscles are soft, and readily undergo changes. Many conditions, such as cholæmia, poisoning with substances which dissolve the corpuscles, and a markedly venous condition of the blood, affect the corpuscles. Interesting observations may be made on the blood in infectious diseases, hæmoglobinuria, and in cases of burning. In anæmia and fever, the capacity for resistance seems to be diminished.

6. FORM AND SIZE OF THE BLOOD-CORPUSCLES OF ANIMALS.—

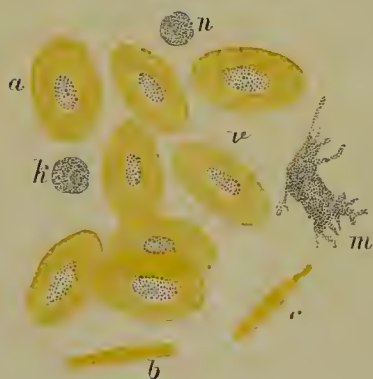


Fig. 11.

Blood of frog. *a*, red-blood corpuscle seen on the flat, *b* in profile, *c* three-quarter face; some of the red corpuscles show vacuoles (*v*); *n*, colourless corpuscle at rest; *m*, one with amœboid processes.

“*alcool au tiers*” (fig. 9, *g*).] It is evident that the larger the blood-corpuscles are the smaller must be the number and total superficies of the corpuscles in a given volume of blood. In birds, however, the number is relatively larger than in other classes of vertebrates, notwithstanding the larger size of their corpuscles; this, doubtless, has a relation to the very energetic metabolism that takes place in birds (*Malassez*). Amongst mammals, carnivora have more blood-corpuscles than herbivora. Goat's blood contains 9,720,000 corpuscles per cubic millimetre; llama's, 13,000,000; bullfinch's, 3,600,000; lizard's, 1,420,000; frog's, 404,000; and that of proteus, 36,000 (*Weleker*). In hibernating animals the number diminishes from 7,000,000 to 2,000,000 per cubic millimetre. No relation exists between the size of the animal and that of its blood-corpuscles.

The invertebrata generally have colourless blood, with colourless corpuscles; but the earth-worm and the larvæ of the large gnats, &c., have red blood whose plasma contains hæmoglobin, while the blood-corpuscles themselves are colourless. Many invertebrates possess red, violet,

All mammals (with the exception of the camel, llama, alpaca, and their allies), and the cyclostomata amongst fishes, *e.g.*, *Petromyzon*, possess circular bi-concave *non-nucleated* disc-shaped coloured corpuscles. Elliptical corpuscles without a nucleus are found in the above-named mammals, while all birds, reptiles, amphibians (fig. 1, B, 1, 2), and fishes (except cyclostomata) have *nucleated* elliptical bi-convex corpuscles (fig. 11). [The corpuscles have a yellow colour, and are transparent. The area occupied by the nucleus is less coloured than the homogeneous perinuclear part].

Amongst vertebrates amphioxus has colourless blood. The large blood-corpuscles of many amphibia, *e.g.*, amphinma, are visible to the naked eye. The blood-corpuscles of the frog (fig. 11) contain, in addition to a nucleus, a nucleolus (*Auerbach*, *Ranvier*), [and the same is true of the coloured corpuscles of the newt (*Stirling*)]. The nucleolus is revealed by acting on the corpuscles with dilute alcohol (1, alcohol; 2, water; *Ranvier's*

brown, or green opalescent blood with colourless corpuscles (amœboid cells). In cephalopods, and some crabs the blood is blue, owing to the presence of a colouring matter (hæmocyanin), which contains copper, and combines with O.

Size ($\mu = 0.001$ Millimetre)				
Of the Disc-shaped Corpuscles.		Of the Elliptical Corpuscles.		
		Short Diameter.		Long Diameter.
Elephant, . . .	9.4 μ	Llama, . . .	4.0 μ	8.0 μ
Man, . . .	7.7 "	Dove, . . .	6.5 "	14.7 "
Dog, . . .	7.3 "	Frog, . . .	15.7 "	22.3 "
Rabbit, . . .	6.9 "	Triton, . . .	19.5 "	29.3 "
Cat, . . .	6.5 "	Proteus, . . .	35.0 "	58.0 "
Sheep, . . .	5.0 "	The corpuscles of Amphiuma are nearly one-third larger than those of Proteus (<i>Riddell</i>).		
Goat, . . .	4.1 "			
Musk-deer, . . .	2.5 "			

7. ORIGIN OF THE RED BLOOD-CORPUSCLES.—(A) **During Embryonic Life.**—Blood-corpuscles are developed in the fowl during the first days of embryonic life. [They appear in groups within the large branched cells of the mesoblast, in the vascular area of the blastoderm outside the developing body of the chick, where they form the "**blood-islands**" of Pander. The mother-cells form an irregular network by the union of the processes of adjoining cells, and meantime the central masses split up, and the nuclei multiply. The small nucleated masses of protoplasm, which represent the blood-corpuscles, acquire a reddish hue, while the surrounding protoplasm, and also that of the processes, becomes vacuolated or hollowed out, constituting a branching system of canals; the outer part of the cells remaining with their nuclei to form the walls of the future blood-vessels. A fluid appears within this system of branched canals in which the corpuscles lie, and gradually a communication is established with the blood-vessels developed in connection with the heart. According to Klein, the nuclei of the protoplasmic wall also proliferate, and give rise to new cells, which are washed away to form blood-corpuscles.] At first the corpuscles exhibit amœboid movements, are devoid of pigment, nucleated, globular, larger and more irregular than the permanent corpuscles. They become coloured, retain their nucleus, and are capable of undergoing multiplication by division; Remak observed all the stages of the process of *division*, which is best seen from the 3rd to the 5th day of incubation. Increase by division also takes place in the larvæ of the salamander, triton, and toad (*Flemming*); and during the intra-uterine life of a mammal, in the spleen, bone-marrow, the liver, and the circulating blood (*Bizzozero*).

Neumann found in the **liver** of the embryo protoplasmic cells containing red blood-corpuscles. Cells, some with, others without, hæmoglobin, but with large nuclei, have been found. These cells increase by division, their nucleus shrivels, and they ultimately form blood-corpuscles (*Löwit*). The **spleen** is also regarded as a centre of their formation, but this seems to be the case only during embryonic life (*Neumann*). Here the red corpuscles are said to arise from yellow, round, nucleated cells, which represent transition forms. Foa and Salvioli found red corpuscles forming endogenously within large protoplasmic cells in **lymphatic glands**. In the later period of embryonic life the characteristic non-nucleated corpuscles seem to be developed from the nucleated corpuscles. The nucleus becomes smaller and smaller, breaks up, and gradually disappears. In the human embryo at the fourth week only nucleated corpuscles are found; at the third month their number is still $\frac{1}{4}$ – $\frac{1}{8}$ of the total corpuscles, while at the end of foetal

life nucleated blood-corpuscles are very rarely found. Of course, in animals with nucleated blood-corpuscles the nucleus of the embryonic blood-corpuscles remains.

(B) **During Post Embryonic Life.**—Kölliker assumed that in the tail of the tadpole capillaries are formed by the anastomoses of the processes of branched and radiating connective-tissue corpuscles. These corpuscles lose their nuclei and protoplasm, become hollowed out, join with neighbouring capillaries, and thus form new blood-channels. J. Arnold and Golubew oppose this view, asserting that the blood-capillaries in the tail of the tadpole give off solid buds at different places, which grow more and more into the surrounding tissues, and anastomose with each other; after their protoplasm and contents disappear, they become hollow, and a branched system of capillaries is formed in the tissues. Ranvier noticed the same mode of growth in the omentum of newly-born kittens.

Young rabbits, a week old, have in their omentum small white or milk spots (*Ranvier*), in which lie "**vaso-formative cells**," i.e., highly refractive cells of variable shape, with long cylindrical protoplasmic processes (fig. 12). In its re-

fractive power the protoplasm of these cells resemble that of lymph-corpuscles. Long rod-like nuclei lie within these cells (K, K), and also *red blood-corpuscles* (r, r), and both are surrounded with protoplasm. These vaso-formative cells give off protoplasmic processes (a, a), some of which end free, while others form a net-work. Here and there elongated connective-tissue corpuscles lie on the branches, and ultimately form the adventitia of the blood-vessel. The vaso-formative cells have many forms: they may be elongated cylinders ending in points, or more round



Fig. 12.

Formation of red blood-corpuscles within "vaso-formative cells," from the omentum of a rabbit seven days old. r, r, the formed corpuscles; K, K, nuclei of the vaso-formative cell; a, a, processes which ultimately unite to form capillaries.

and oval, resembling lymph cells, or modified connective-tissue corpuscles. *These cells are always the seat of origin of non-nucleated red blood-corpuscles*, which arise in the protoplasm of vaso-formative cells, as chlorophyll grains or starch granules arise within the cells of plants. The corpuscles escape and are washed into the circulation, when the cells, by means of their processes, form connections with the circulatory system. Probably the vessels so formed in the omentum are only temporary. May it not be that there are many other situations in the body where blood is regenerated?

[The observations of Schäfer also prove the **intra-cellular origin** of red blood-corpuscles, and although this mode usually ceases before birth, still it is found in the rat at birth. The protoplasm of the subcutaneous **connective-tissue corpuscles**, which are derived from the mesoblast, has in it small coloured globules about the size of a coloured corpuscle. The mother-cells elongate, become pointed at their ends, and unite with processes from adjoining cells. The cells become vacuolated; fluid or plasma, in which the liberated corpuscles float, appears in their interior, and ultimately a communication is established with the general circulation.]

Neumann observed similar formations in the embryonic liver; Wissotzky in the rabbit's annion; Klein in the embryo chick; and Bayerl in ossifying cartilage (p. 8). All these observations go to show that at a certain early period of development blood-corpuscles are formed within other large cells of the mesoblast, and that part of the protoplasm of these blood-forming cells remains to form the wall of the future blood-vessel.

(C) **Later Formation.**—Most observers agree that the red blood-corpuscles are formed from special nucleated cells, which gradually assume the form and colour of the perfect red corpuscle. According to Neumann, however, these corpuscles are pigmented from the first. In the tailed amphibians and fishes, the **spleen**, in all other vertebrates the **red marrow of bone**, are the seats of formation of these corpuscles, which subsequently increase by division (*Neumann, Rindfleisch, Bizzozero*). In the red marrow of bone we can study all the stages of the transformation; especially pale contractile cells similar to colourless corpuscles, and also red nucleated corpuscles, which are similar to the nucleated corpuscles of the embryo, and the progenitors of the red corpuscles. These transition cells are said by Erb to be more numerous after severe hæmorrhage, the number of them occurring in the blood corresponding with the energy of the formative process. After copious hæmorrhage these transition forms appear in numbers in the blood-stream. The small veins, and perhaps the capillaries of the red marrow of bone and the spleen have no proper walls, so that the red corpuscles when formed can pass into the circulation.

Red or blood-forming marrow occurs in the bones of the skull, and in most of the bones of the trunk, while the bones of the extremities either contain yellow marrow (which is essentially fatty in its nature), or, at most, it is only the heads of the long bones that contain red marrow. Where the blood-regeneration process is very active, however, the yellow marrow may be changed into red, even throughout all the bones of the extremities (*Neumann*).

[The most recent observers (*Löwit, Bizzozero, and Denys*), regard the red and white blood-corpuscles as being developed independently of each other. Löwit calls the early stages of the former **erythroblasts** and of the latter **leucoblasts**. In the red marrow of the bones of **birds**, the red corpuscles are developed within the blood-vessels of the marrow, and the colourless ones in the tissue which lies in the vascular meshes. The erythroblasts are originally colourless, and between them and the complete red corpuscle there is a complete series of gradations. The erythroblasts have a large, spherical, central nucleus with a pronounced nuclein network and homogeneous or slightly granular protoplasm. The leucoblasts, on the contrary, contain a small nucleus of variable form, with numerous nucleoli, and often placed peripherally. The protoplasm contains many eosinophile granules. Both exhibit amœboid movement, but this is more active in the leucoblasts. Both divide by mitosis. Some of the erythroblasts pass out directly in the blood-stream, while the leucocytes in virtue of their amœboid movements pass by diapedesis into the vessels. Repeated hæmorrhages lead to rapid mitotic division of both forms.]

[In extra-uterine life, in **mammals**, the **red marrow** of bone is undoubtedly the chief seat of the formation of red blood-corpuscles. In it are to be found a large number of nucleated red blood-corpuscles, *i.e.*, embryonic forms, which ultimately lose their nuclei, pass into the circulation as perfect red corpuscles. After copious hæmorrhage, when the animal forms a larger number of corpuscles than usual, as it were striving to make up the deficiency, the number of nucleated red corpuscles in the red blood-forming marrow is greatly increased, and even parts of what was previously yellow marrow appear somewhat reddish. The blood-forming function of the red marrow is greatly increased after hæmorrhage (*Neumann and Bizzozero*). Often, however, there is an additional factor, as shown by Bizzozero and Salvioli in the case of guinea-pigs and dogs. In these animals after severe anæmia, due to repeated hæmorrhages, the spleen also participates in the formation of red corpuscles, for in it are found nucleated red corpuscles similar to those of the red marrow.]

[In **birds** also red blood-corpuscles are formed in the red marrow, but so far as the spleen has been investigated, Bizzozero has not found any reason to believe that this organ is concerned in the formation of red blood-corpuscles in these animals.]

[According to Bizzozero, there is no evidence to show that the white corpuscles are precursors of the red; the red corpuscles are derived from special corpuscles (erythroblasts), and so are the white (leucoblasts). The red ones seem to be

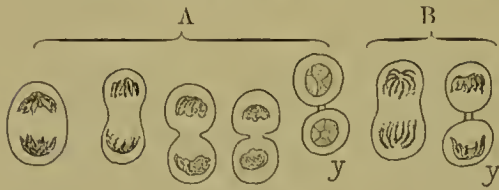


Fig. 13.

A, Red blood-corpuscle of a chick undergoing mitotic division at 5th-6th day of incubation.

B, red blood-corpuscle of frog dividing; Y shows a thin colourless thread of protoplasm still connecting the two daughter corpuscles.

formed within the blood-vessels of the red marrow and the colourless ones in the extra-vascular parts of the marrow. The red corpuscles are formed by the mitotic division of pre-existing cells, which are quite different from the colourless corpuscles; their protoplasm is never granular, but almost always homogeneous, never colourless, but slightly tinged by hæmoglobin; they never exhibit the lively amœboid movements of the white corpuscles. If the red marrow of any of the classes of the vertebrata be examined, especially after repeated hæmorrhages—there will always be found numerous erythroblasts undergoing mitosis (fig. 13).]

[In all classes of the Vertebrata, then, the red marrow is the great seat of the formation of red corpuscles during adult life. But how is it during the development of the young animals? It is not necessary to assume that the red are derived from the colourless corpuscles. If we study the fate of the red corpuscles we find that their presence is not due absolutely to any one organ. In the first phases of embryonic life, the red corpuscles develop and divide within the whole vascular system. At a later period this ceases and they are developed in the liver and spleen; at a later period still—in extra-uterine life—and when the bone marrow is greatly developed the blood-forming activity of the liver and spleen is gradually diminished and ceases. But the loss is not absolute in the case of the last organ, as it can again be caused to produce red corpuscles after copious hæmorrhage. The blood-plates are in no way concerned in the formation of red corpuscles, they have to do with the coagulation and other vital phenomena of the blood.]

[The balance of evidence points to the formation of red blood-corpuscles in extra-uterine life—both in animals with nucleated and in those with non-nucleated corpuscles—by the same process as in embryonic life (*i.e.*, by **indirect division** or **mitosis** of a typical cellular element, which during extra-uterine life is chiefly found in the marrow of bone (*Bizzozero*).]

8. DECAY OF THE RED BLOOD-CORPUSCLES.—The blood-corpuscles undergo decay within a limited time, and the **liver** is regarded as one of the chief organs in which their disintegration occurs, because bile-pigments are formed from hæmoglobin, and the blood of the hepatic vein contains fewer red corpuscles than the portal vein.

The **splenic pulp** contains cells which indicate that coloured corpuscles are broken up within it. These are the so-called “blood-corpuscle containing cells” (§ 103). Quincke’s observations go to show that the red corpuscles—which may live from three to four weeks—when about to disintegrate, are taken up by the white blood-corpuscles in the hepatic capillaries, by the cells of the spleen and the bone-marrow, and are stored up chiefly in the **capillaries of the liver**, in the **spleen**, and in the **marrow of bone**. They are transformed partly into coloured, and partly into colourless proteids which contain iron, and are either deposited in a granular form, or are dissolved. Part of the products of decomposition is used for the formation of new blood-corpuscles in the marrow and in the spleen, and also perhaps in the liver, while a portion of the iron is excreted by the liver in the bile.

That the normal red blood-corpuscles and other particles suspended in the blood-stream are not taken up in this way, may be due to their being smooth and polished. As the corpuscles grow older and become more rigid, they, as it were are caught by the amœboid cells. As cells containing blood-corpuscles are very rarely found in the general circulation, one may assume that the occurrence of these cells within the spleen, liver, and marrow of bone is favoured by the slowness of the circulation in these organs (*Quincke*).

Pathological.—In certain pathological conditions, ferruginous substances derived from the red blood-corpuscles are found in masses in the spleen, the marrow of bone, and the capillaries of the liver:—(1) When the disintegration of blood-corpuscles is increased, as in anæmia (*Stahel*). (2) When the formation of red blood-corpuscles from the old material is diminished. If the excretion from the liver cells be prevented, iron accumulates within them; it is also more abundant in the blood-serum, and it may even accumulate in the secretory cells of the cortex of the kidney and pancreas, in gland cells, and in the tissue elements of other organs. When the amount of blood in dogs is greatly increased, after four weeks an enormous number of granules containing iron occur in the leucocytes of the liver capillaries, the cells of the spleen, bone-marrow, lymph-glands, liver cells, and the epithelium of the cortex of the kidney. The iron reaction in the last two situations occurs after the introduction of hæmoglobin, or of salts of iron into the blood (*Glæveck, v. Stark*.) In thrombi and in extravasations of blood into the neighbourhood of living tissues, there is formed besides hæmatoidin, the body hæmatosiderin.

When we reflect how rapidly large quantities of blood are replaced after hæmorrhage and after menstruation, it is evident that there must be a brisk manufactory somewhere. As to the number of corpuscles which daily decay, we have in some measure an index in the amount of bile-pigment and urine-pigment resulting from the transformation of the liberated hæmoglobin (§ 20).

9. II. COLOURLESS CORPUSCLES, BLOOD-PLATES, AND GRANULES.—

White Blood-Corpuscles.—Blood, like many other tissues, contains a number of

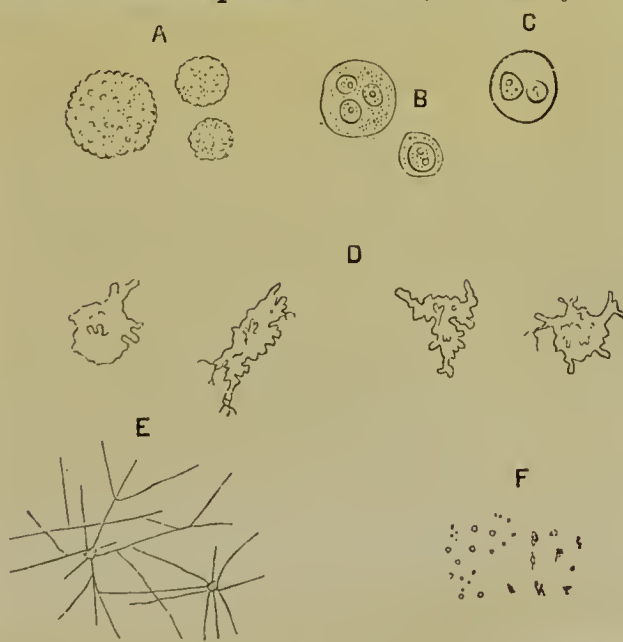


Fig. 14.

A, human white blood-corpuscles, without any reagent; B, after the action of water; C, after acetic acid; D, frog's corpuscles, changes of shape due to amœboid movement; E, fibrils of fibrin from coagulated blood; F, elementary granules.

cells or corpuscles which reach it from without; the corpuscles vary somewhat in form, and are called **colourless or white blood-corpuscles** or "**leucocytes**" (*Hewson, 1770*). Similar corpuscles are found in lymph, adenoid tissue, marrow of bone, and as wandering cells or leucocytes in connective-tissue, and also between glandular and epithelial cells [so that their ubiquity is a marked feature, thus differing from the coloured corpuscles which normally remain within the blood-vessels]. So that these corpuscles are by no means peculiar to blood alone. They all consist of more or less spherical masses of protoplasm, which is sticky, highly refractile, soft, capable of movement, and devoid of an envelope (fig. 14). When they are quite fresh (A) it is difficult to detect the nucleus, but after they have been shed for some time, or after

the addition of water (B) or acetic acid, the nucleus (which is usually a compound one) appears; acetic acid clears up the perinuclear protoplasm, and reveals the presence of the nuclei, of which the number varies from one to four, although generally three are found. The subsequent addition of magenta solution causes the nuclei to stain deeply. Water makes the contents more turbid, and

causes the corpuscles to swell up. One or more nucleoli may be present in the nucleus. The **size** of the corpuscles varies from 4–13 μ , and as a rule they are about $\frac{1}{2500}$ of an inch in diameter; in the smallest forms the layer of the protoplasm is extremely thin. They all exhibit **amœboid movements**, which are very apparent in the larger corpuscles, and were discovered by Wharton Jones in the skate (1846), and by Davine in the corpuscles of man (1850). Max Schultze describes three different forms in **human blood** :—

(1) The smallest, spherical forms, less than the red corpuscles, with one or two nuclei, and a very small amount of protoplasm.

(2) Spherical forms, the same size as the coloured blood-corpuscles.

(3) The large amœboid corpuscles, with much protoplasm and distinctly evident movements.

[On examining human blood microscopically, more especially after the coloured blood-corpuscles have run into rouleaux, the colourless corpuscles may readily be detected, there being usually three or four of them visible in the field at once (fig. 5). They adhere to the glass slide, for if the cover-glass be moved, the coloured corpuscles readily glide over each other, while the colourless can be seen still adhering to the slide.]

[**White Corpuscles of Newt's Blood.**—The characters of the colourless corpuscles are best studied in a drop of newt's blood, which contains the following varieties :—

(1) **The large finely granular corpuscle**, which is about $\frac{1}{1100}$ of an inch in diameter, irregular in outline, with fine processes or pseudopodia projecting from its surface. It rapidly changes its shape at the ordinary temperature, and in its interior a bi- or tri-partite nucleus may be seen, surrounded with fine granular protoplasm, whose outline is continually changing. Sometimes *vacuoles* are seen in the protoplasm.

(2) **The coarsely granular variety** is less common than the first-mentioned, but when detected its characters are distinct. The protoplasm contains, besides a nucleus, a large number of highly refractive granules, and the corpuscle usually exhibits active amœboid movements; suddenly the granules may be seen to rush from one side of the corpuscle to the other. The processes are usually more blunt than those emitted by (1). The relation between these two kinds of corpuscles has not been ascertained.

(3) **The small colourless corpuscles** are more like the ordinary human colourless corpuscle, and they too exhibit amœboid movements.]

Two kinds of colourless corpuscles like (1) and (2) exist in **frog's blood**. In the coarsely-granular corpuscles the glancing granules may be of a fatty nature, since they dissolve in alcohol and ether, but other granules exist which are insoluble in these fluids. The nature of the latter is unknown. Very large colourless corpuscles exist in the axolotl's blood.

[In the blood of **birds** there are four varieties of colourless corpuscles :—

(1) Leucocytes of 7–8 μ in diameter, very numerous, which exhibit lively movements, and send out processes; the protoplasm is tolerably dark, but this is not due to granules as in the case of the leucocytes of mammals, but to the presence of **glancing crystals**, which are usually pointed at their ends, and arranged radially from the centre to the periphery of the corpuscles. They are not fatty in their nature.

(2) Leucocytes about the size of (1), but with spherical fine granules. They are nucleated, contractile, but the latter to a less degree than (1).

(3) Small (5–6 μ in diameter) finely granular leucocytes, which are contractile, but do not send out processes.

(4) Colourless cells, having an oval nucleolated refractive nucleus, and the protoplasm of the cell vacuolated. They do not exhibit contractile movements. The last variety was regarded by Hayem as corpuscles that developed into red corpuscles, but there is no evidence confirmatory of this view] (*Bizzozzero*).

[**Action of Reagents on the Colourless Corpuscles.**—(a) **Water**, when added slowly, causes the colourless corpuscles to become globular, and the granules within them to exhibit Brownian movements (fig. 14B). (b) **Pigments**, such as magenta or carmine, stain the nuclei very deeply, and the protoplasm to a less extent. (c) **Dilute Acetic Acid** clears up the surrounding protoplasm and brings clearly into view the composite nucleus, which may be stained thereafter with magenta. (d) **Iodine** gives a faint port-wine colour, especially in horse's blood, indicating the presence of glycogen. (e) **Dilute Alcohol** causes the formation of clear blebs on the surface of the corpuscles, and brings the nuclei into view (*Ranvier, Stirling*).]

[A delicate plexus of fibrils—**intra-nuclear plexus**—exists within the nucleus just as in other cells. It is very probable that the protoplasm itself is pervaded by a similar plexus of fibrils, and that it is continuous with the intra-nuclear plexus (fig. 15).] The colourless corpuseles divide by mitosis, and in this way reproduce themselves.

The **Number of Colourless Corpuseles** is very much less than that of the red corpuseles, and is subject to considerable variations. It is certain that the colourless corpuseles are *very much fewer in shed blood* than in blood still within the blood-vessels. Immediately after blood is shed an enormous number of white corpuseles disappear (§ 30).



Fig. 15.

Plexus of fibrils in a colourless blood-corpuscle.

Al. Schmidt estimates the number that remain at $\frac{1}{10}$ of the whole originally present in the circulating blood. The proportion is greater in children than in adults. The following table gives the number in shed blood :—

NUMBER OF WHITE IN PROPORTION TO RED BLOOD-CORPUSCLES.		
In Normal Condition.	In Different Places.	In Different Conditions.
1 : 335 (<i>Welcker</i>). 1 : 357 (<i>Moleschott</i>).	Splenic Vein, 1 : 60 Splenic Artery, 1 : 2,260 Hepatic Vein, 1 : 170 Portal Vein, 1 : 740 Generally more numerous in Veins than Arteries.	<i>Increased</i> by Digestion, Loss of Blood, Prolonged Suppuration, Parturition, Leukæmia, Quinine, Bitters. <i>Diminished</i> by Hunger, Bad Nourishment.

[The number also varies with the **Age and Sex** :—

Age. Sex.	White. Red.	General Conditions.	White. Red.
Girls, ...	1 : 405	While fasting, . . .	1 : 716
Boys, ...	1 : 226	After a meal	1 : 347
Adults, ...	1 : 334	During pregnancy, .	1 : 281]
Old Age, ...	1 : 381		

The **amœboid movements** of the white corpuseles (so called because they resemble the movements of amœba) consist in an alternate contraction and relaxation of the protoplasm surrounding the nucleus. Proeesses are pushed out from the surface, and are retracted again (fig. 16). There is an *internal current* in the protoplasm, and the nucleus has also been observed to change its form [and exhibit contractions without the corpusele dividing. The mitotic aster, and convolution of the intra-nuclear plexus have been seen]. Two series of phenomena result from these movements :— (1) The “**wandering**” or locomotion of the corpuseles due to the extension and retraction of their proeesses ; (2) the **absorption of small particles** into their interior (fat, pigment, foreign bodies). The partielees

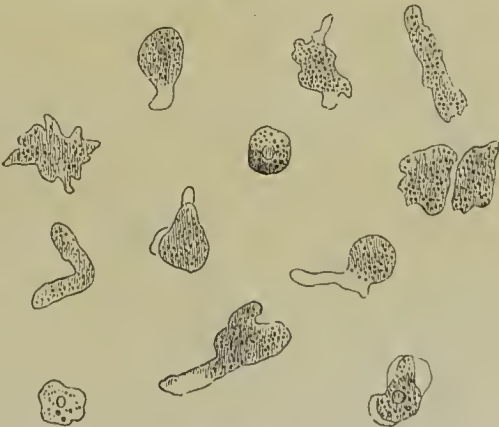


Fig. 16.

Human leucocytes showing amœboid movements.

adhere to the sticky external surface, are carried into the interior by the internal currents, and may eventually be excreted, just as particles are taken up by amœba and the effete particles excreted. [Max Schultze observed that coloured particles were readily taken up by these corpuscles. **Conditions for movement.**—In order that the amœboid movements of the leucocytes may take place, it is necessary that there be—(1) a certain temperature and normal atmospheric pressure; (2) the surrounding medium, within certain limits, must be “indifferent,” and contain a sufficient amount of water and oxygen; (3) there must be a basis or support to move on.]

Effect of Reagents.—On a hot stage (35°–40° C.) the colourless corpuscles of **warm-blooded animals** retain their power of moving for a long time; at 40° C. for two to three hours; at 50° C. the proteids are coagulated and cause “**heat rigor**” and death, [when their movements no longer recur on lowering the temperature]. In **cold-blooded animals** (frogs), colourless corpuscles may be seen to crawl out of small coagula, in a moist chamber, and move about in the serum. [Draw a drop of newt’s blood into a capillary tube, seal up the ends of the latter and allow the blood to coagulate. After a time, examine the tube in clove oil, when some of the colourless corpuscles will be found to have made their way out of the clot.] **Induction shocks** cause them to withdraw their processes and become spherical, and, if the shocks be not too strong, their movements recommence. Strong and continued shocks kill them, causing them to swell up, and completely disintegrating them.

Diapedesis.—These amœboid movements are of special interest on account of the “wandering out” (diapedesis) of colourless blood-corpuscles through the walls of the blood-vessels (§ 95).

[**Effect of Drugs.**—Acids and alkalies, if very dilute, at first increase, but afterwards arrest their movements. **Sodic chloride** in a 1 per cent. solution at first accelerates their movements, but afterwards produces a tetanic contraction, and, it may be, expulsion of any food particles they contain. The **Cinchona alkaloids**—quinine, quinidine, cinchonidine (1 : 1500)—quickly arrest the locomotive movements, as well as the protrusion of pseudopodia, although the leucocytes of different animals vary somewhat in their resistance to the action of drugs. Quinine not only arrests the movements of the leucocytes when applied to them directly, but when injected into the circulation of a frog the leucocytes no longer pass through the walls of the capillaries (*Binz*).]

The chyle contains leucocytes, which are more resistant than those of the blood, but less so than those of the coagulable transudations. The leucocytes of the lymphatic glands may also be dissolved (*Rauschenbach*).

Relation to Aniline Pigments.—Ehrlich has observed a remarkable relation of the white corpuscles to *acid* (eosin, picric acid, aurantia), *basic* (dahlia, acetate of rosanilin), or *neutral* (picrate of rosanilin) reactions. The smallest protoplasmic granules of the cells have different chemical affinities for these pigments. Thus Ehrlich distinguishes “**eosinophile**,” “**basophile**,” and “**neutrophile**” granules within the cells. *Eosinophile* granules occur in the leucocytes which come from bone-marrow, the myelogenic leucocytes. The small leucocytes, *i.e.*, those about the size of a coloured blood-corpuscle or slightly larger, are formed in the lymphatic glands, the lymphogenic. The large amœboid multi-nucleated cells, which are found outside the vessels in inflammation, exhibit a neutrophile reaction. Their origin is unknown, and so is that of the large uni-nucleated cells, and the large cells with constricted nuclei. The eosinophile corpuscles are considerably increased in leukæmia. The *basophile* granules occur also in connective-tissue corpuscles, especially in the neighbourhood of epithelium; they are always greatly increased where chronic inflammation occurs.

Struggle between Microbes and the Organism.—Metschnikoff emphasizes the activity of the leucocytes in retrogressive processes, whereby the parts to be removed are taken up by them in fine granules, and, as it were, are “*caten*.” Hence, he calls such cells “**phagocytes**.” They may be found in the atrophied tails of batrachians, the cells containing in their interior whole pieces of nerve-fibre and primitive muscular bundles. Schizomycetes which have found their way into the blood (§ 184) have been found to be partly taken up by the colourless corpuscles. [The spores of a kind of yeast are similarly attacked in the transparent tissues of the water-flea by the leucocytes, and the connective-tissue cells also destroy microbes.]

[It must not be forgotten in this connection that albumoses are produced by various microbes, and that these soluble products are capable when injected into an animal of producing immunity

against the attack of certain microbes, *i.e.*, a chemical as distinguished from a vaccinal immunity (§ 166).]

III. **Blood-Plates.**—Special attention has recently been directed to a *third* element of the blood, the “**blood-plates**,” “**blood-platelets**,” or “**blood-tablets**” of Bizzozero (figs. 17 and 18); pale, colourless, oval, round, or lenticular discs of variable size (mean 3μ). In a healthy man Fusari found 18,000 to 250,000 in 1 cubic millimetre of blood. These blood-plates may be recognised in the circulating blood of the mesentery of a chloralised guinea-pig and the wing of the bat.



Fig. 17.

“Blood-plates” and their derivatives. 1, a red blood-corpuscle on the flat; 2, on the side; 3, unchanged blood-plates; 4, lymph-corpuscle, surrounded by blood-plates; 5, altered blood-plates; 6, lymph-corpuscle with two heaps of fused blood-plates and threads of fibrin; 7, group of fused blood-plates; 8, small group of partially dissolved blood-plates with fibrils of fibrin.

They are precipitated in enormous numbers upon threads suspended in fresh shed blood [or if blood be beaten with a linen thread]. They may be obtained from blood flowing directly from a blood-vessel, on mixing it with one per cent. solution of osmic acid. They rapidly change in shed blood (fig. 17, 5), disintegrating, forming small particles, and ultimately dissolving. When several occur together they rapidly unite, form small groups (7), and collect into finely granular masses. These masses may be associated in coagulated blood with fibrils of fibrin (fig. 17).

[These blood-plates are best seen in the shed blood of the guinea-pig, especially if it be mixed with a solution of sodic sulphate (sp. gr. 1022) or $\frac{1}{4}$ per cent. NaCl tinged with methyl-violet. Bizzozero regards them as the agents which immediately induce coagulation and take part in the formation of fibrin during coagulation of the blood; Eberth and Schimmelbusch ascribe the initial formation of white thrombi to them. According to Löwit they are formed from partially disintegrated leucocytes, as a consequence of alteration of the blood. Along with the leucocytes they are concerned in the formation of fibrin (*Hlava*). These structures were known to earlier observers; but their significance has been variously interpreted. Hayem called them *hæmatoblasts*. Halla found that they increased in pregnancy, Afanassiew in conditions of regeneration of the blood, and Fusari in febrile anæmia; they are diminished in fever.

[As to the *hæmatoblasts*, or, as they have also been called, the “globules of Donuë” by Pouchet, there seems to be some confusion, for both coloured and colourless granules are described under these names. As Gibson suggests, the former are, perhaps, parts of disintegrated coloured corpuscles, whilst the latter are the blood-plates. The “invisible blood-corpuscles” described by Norris seem to be simply decolorised red corpuscles (*Hart, Gibson*).]

[If frogs be bled repeatedly, thus leading to active blood-formation, it is stated that on the third to the sixth day all stages of mitotic division of the blood-platelets are to be seen (*Mondino*). The same observer has described mitosis of mammalian blood-platelets. These observations, however, have still to be confirmed]

IV. Elementary Granules.—Blood contains elementary granules (fig. 14, F),

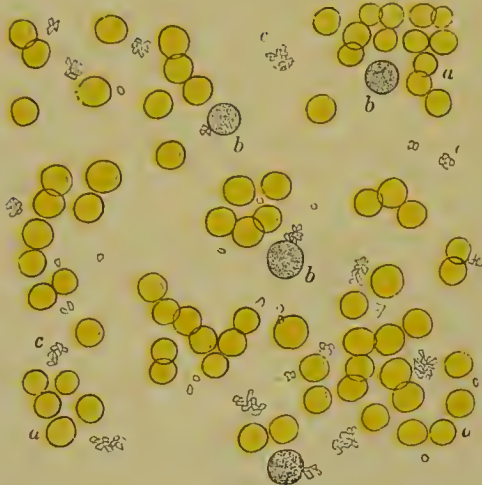


Fig. 18.

Blood-corpuscles and blood-plates from normal human blood. (a) Red blood-corpuscles; (b) colourless corpuscles; (c) blood-plates.

[i.e., the elementary particles of Zimmermann and Beale. They are irregular bodies, much smaller than the ordinary corpuscles, and appear to consist of masses of protoplasm detached from the surface of leucocytes, or derived from the disintegration of these corpuscles or of the blood-plates. Others, again, are completely spherical granules, either consisting of some proteid substance or fatty in their nature. The protoplasmic and the proteid granules disappear on the addition of acetic acid, while the fatty granules (which are most numerous after a diet rich in fats) dissolve in ether.]

V. In coagulated blood, delicate threads of fibrin (figs. 14, E, and 17, 6, 7, 8) are seen, more especially after the corpuscles have run into rouleaux. At the nodes of these fibres are found granules which closely resemble those described under III.

[When the blood-forming process is particularly active, as after repeated hæmorrhages, “nucleated coloured corpuscles” or the “corpuscles of Neumann” are sometimes found in the blood. They are identical with the nucleated coloured blood-corpuscles of the fœtus, being somewhat larger than the non-nucleated coloured corpuscle (§ 7).]

10. ABNORMAL CHANGES OF THE BLOOD-CORPUSCLES.—(1) Hæmorrhages diminish the number of red corpuscles (at most one-half), and so does menstruation. The loss is partly covered by the absorption of fluid from the tissues. Menstruation shows us that a moderate loss of red corpuscles is replaced within twenty-eight days. When a large amount of blood is lost, so that all the vital processes are lowered, the time may be extended to five weeks. In acute fevers, as the temperature increases, the number of red corpuscles diminishes, while the white corpuscles increase in number. By greatly cooling peripheral parts of the body as by keeping the hands in iced water, in some individuals possessing red blood-corpuscles of low resisting power, these corpuscles are dissolved, the blood-plasma is reddened, and even hæmoglobinuria may occur (§ 265).

Diminished production of new red corpuscles causes a decrease, since blood-corpuscles are continually being used up. In chlorotic females there seems to be a congenital weakness in the blood-forming and blood-propelling apparatus, the cause of which is to be sought for in some faulty condition of the mesoblast. In them the heart and the blood-vessels are small, and the absolute number of corpuscles may be diminished one-half, although the relative number may be retained, while in the corpuscles themselves the hæmoglobin is diminished almost one-third; but it rises again after the administration of iron (Hayem). The administration of iron increases the amount of hæmoglobin in the blood. [The action of iron in anæmic persons has been known since the time of Sydenham. Hayem also finds in certain forms of anæmia that there is considerable variation in the size of the red corpuscles, and that in chronic anæmia the mean diameter of the corpuscles is always less than normal (7μ to 6μ). There is, moreover, a persistent alteration in the volume, colouring power, and consistence of the corpuscles, consequently a want of accord between the number of the corpuscles and their colouring power, i.e., the amount of hæmoglobin which they contain. In pernicious anæmia, in which the continued decrease in the red corpuscles may ultimately produce death, there is undoubtedly a severe affection of the blood-forming apparatus. The corpuscles assume many abnormal and bizarre forms, often being oval or tailed, irregularly shaped, and sometimes very pale; while numerous cells containing blood-corpuscles are found in the marrow of bone. In this disease, although the red blood-corpuscles are diminished in number, some may be larger and contain more hæmoglobin than normal corpuscles. The number of coloured corpuscles is also diminished in chronic poisoning by lead or miasmata, and also by the poison of syphilis.]

(2) The size of the corpuscles varies in disease from 2.9 – 12.9μ (mean 6 – 8μ); “dwarf corpuscles” or microcytes (6μ and less) are regarded as young forms, and occur plentifully in nearly all cases of anæmia. “Giant blood-corpuscles” or macrocytes (10μ and more) are constant in pernicious anæmia, and sometimes in leucæmia, chlorosis, and liver cirrhosis (Gram).

(3) **Abnormal forms** of the red corpuscles have been observed after severe burns (*Lesser*) ; the corpuscles are much smaller, and under the influence of the heat particles seem to be detached from them, just as can be seen happening under the microscope as the effect of heat (p. 7). **Disintegration of the corpuscles** into fine droplets has been observed in various discases, as in severe malarial fevers. The dark granules of a pigment closely related to hematin are derived from the granules arising from the disintegration of the blood-corpuscles, and these particles float in the blood (*melanæmia*). This condition can be produced artificially by injecting bisulphide of carbon (7 to 10 of oil) subcutaneously into rabbits (*Schwalbe*). They are partly absorbed by the colourless corpuscles, but they are also deposited in the spleen, liver, brain, and bone-marrow.

(4) Sometimes the red corpuscles are abnormally soft, and readily yield to pressure.

Parasites of blood-corpuscles—Within the red blood-corpuscles of birds, fishes, and tortoises, parasites are occasionally developed in the form of round "pseudo-vacuoles" from which free parasites are subsequently discharged (*Danilevsky*). In malarial conditions in man, protozoon-like organisms have been seen within the red corpuscles, the *plasmodium malariae* (*Marchiafava*).

The **white corpuscles** are enormously increased in number in *leukæmia* (*J. H. Bennett, Virchow*). In some cases the blood looks as if it were mixed with milk. The colourless corpuscles seemed to be formed chiefly in bone-marrow (*E. Neumann*), and also in the spleen and lymphatic glands (myelogenic, splenic, and lymphatic leukæmia).

11. CHEMICAL CONSTITUENTS OF THE RED BLOOD-CORPUSCLES.—(1)

The colouring matter or hæmoglobin (Hb) is the cause of the red colour of blood; it also occurs in muscle and in traces in the fluid part of blood, but in the last case only as the result of the solution of some red corpuscles. Its **percentage composition** is, according to Hüfner, in the blood of the pig (and ox in brackets), C 54·71 (54·66), H 7·38 (7·25), N 17·43 (17·70), S 0·479 (0·447), Fe 0·399 (0·40), O 19·602 (19·543). Its rational formula is unknown, but Preyer gives the empirical formula $C_{600}, H_{960}, N_{154}, Fe, S_3, O_{179}$. Although it is a colloid substance it **crystallises** in all classes of vertebrates, according to the rhombic system, and chiefly in rhombic plates or prisms; in the guinea-pig in rhombic tetrahedra; in the squirrel, however, it yields hexagonal plates. The varying forms, perhaps, correspond to slight differences in the chemical composition in different cases. Crystals separate from the blood of all classes of vertebrata during the slow evaporation of lake-coloured blood, but with varying facility (fig. 19).



Fig. 19.

Hæmoglobin crystals from blood. *a, b*, human; *c*, cat; *d*, guinea-pig; *e*, hamster; *f*, squirrel.

[The following analysis shows the composition of the hæmoglobin of the horse and dog, so that they do not seem to be quite identical in composition.]

Hæmoglobin of Horse.

C 51·15
H 6·76
N 17·94
S 0·390
Fe 0·335
O 23·43 (*Zinoffsky*).

Hæmoglobin of Dog.

53·91
6·62
15·98
0·542
0·333
22·62 (*Jaquel*).]

The colouring matter crystallises with great difficulty from the blood of the calf, pig, pigeon, and frog; with difficulty from that of man, monkey, rabbit, and sheep; readily from that of the dog,

cat, mouse, and horse; and very readily from that of the rat and guinea-pig (*Preyer*). [Copeman finds that coloured crystals can be obtained from the blood of the frog. More rarely a crystal is formed from a single corpuscle enclosing the stroma. Crystals have been found near the nucleus of the large corpuscles of fishes, and in this class of vertebrates colourless crystals have been observed. Crystals of hæmoglobin are readily found in the prepared blood of the salamander.]

Dichroism.—Hæmoglobin crystals are doubly refractive and pleo-chromatic; they are bluish-red with transmitted light, scarlet-red by reflected light. They contain from 3 to 9 per cent. water of crystallisation, and are soluble in water, but more so in dilute alkalis. They are insoluble in alcohol, ether, chloroform, and fats. The solutions are dichroic; red in reflected light, and green in transmitted light. In contact with protoplasmic cells, *e.g.* leucocytes, hæmoglobin is destroyed in five days and regenerated again after twelve days (*Schwartz*).

In the act of crystallisation the hæmoglobin seems to undergo some internal change. Before it crystallises it does not diffuse like a true colloid, and it also rapidly decomposes hydric peroxide. If it be redissolved after crystallisation, it diffuses, although only to a small extent, but it no longer decomposes hydric peroxide, and is decolorised by it. [The presence of O favours crystallisation.]

12. PREPARATION OF HÆMOGLOBIN CRYSTALS.—Method of Rollett.—Put defibrinated blood in a platinum capsule placed on a freezing mixture, freeze the blood, and then thaw it; pour the lake-coloured blood into a plate until it forms a stratum not more than $1\frac{1}{2}$ mm. in thickness and allow it to evaporate slowly in a cool place, when crystals will separate.

Method of Hoppe-Seyler.—Mix defibrinated blood with 10 volumes of a 20 per cent. salt solution, and allow it to stand for two days. Remove the clear upper fluid with a pipette, wash the thick deposit of blood-corpuscles with water, and afterwards shake it for a long time with an equal volume of ether, which dissolves the blood-corpuscles. Remove the ether, filter the lake-coloured blood, add to it $\frac{1}{4}$ of its volume of cold alcohol (0°), and allow the mixture to stand in the cold for several days. The numerous crystals can be collected on a filter and pressed between folds of blotting-paper.

Method of Gscheidlen.—Take defibrinated blood, which has been exposed for twenty-four hours to the air, and keep it in a closed tube of narrow calibre for several days at 37° C. When the blood is spread on glass, the crystals form rapidly. [Vaccine tubes answer very well.]

[Method of Stirling and Brito.]—It is in many cases sufficient to mix a drop of blood with a few drops of water on a glass slide, and to seal up the preparation. After a few days beautiful crystals are developed. The addition of water to the blood of some animals, such as the rat and the guinea-pig, is rapidly followed by the formation of crystals of hæmoglobin. Very large crystals of reduced hæmoglobin may be obtained from the stomach of the leech several days after it has sucked blood.]

[Crystals of Reduced Hæmoglobin] may be obtained from human blood; (1) by the addition to blood of decomposed serum, or of pericardial fluid; (2) treatment with bile, especially the bile of a cat; (3) agitation with ether; (4) semi-digestion in the stomach of the leech (*Stirling, Bond, Copeman*). They may also be obtained as reddish-violet coloured prisms, but green in transmitted light if they are thin, by sealing up some putrefying HbO_2 in a tube in an atmosphere of hydrogen (*Nencki and Sieber*).]

13. QUANTITATIVE ESTIMATION OF HÆMOGLOBIN.—(a) **From the Amount of Iron.**—As dry (100° C.) hæmoglobin contains 0.42 per cent. of iron, the amount of hæmoglobin may be calculated from the amount of iron. If m represents the percentage amount of metallic iron, then the percentage of hæmoglobin in blood is $= \frac{100m}{0.42}$. The procedure is the following:—

Calcine a weighed quantity of blood, and exhaust the ash with HCl to obtain ferric chloride, which is transformed into ferrous chloride. The solution is then titrated with potassic permanganate.

(b) **Colorimetric Method.**—Prepare a dilute watery solution of hæmoglobin crystals of a known strength. With this compare an aqueous dilution of the blood to be investigated, by adding water to it until the colour of the test solution is obtained. Of course, the solutions must be compared in vessels with parallel sides and of exactly the same width, so as to give the same thickness of fluid (*Hoppe-Seyler*). [In the vessel with parallel sides, or **hæmatinometer**, the sides are exactly 1 centimetre apart. Instead of using a standard solution of oxyhæmoglobin, a solution of picro-carminate of ammonia may be used (*Rajewsky, Malassez*).]

(c) **By the Spectroscope.**—Preyer found that a 0.8 per cent. watery solution (1 cm. thick), allowed the red, the yellow, and the first strip of green to be seen (fig. 25, 1). Take the blood to be investigated (about 0.5 c.m.), and dilute it with water until it shows exactly the same optical effects in the spectroscope. If k is the percentage of Hb which allows green to pass

through (0·8 per cent.), b , the volume of blood investigated (about 0·5 c.cm.), w , the necessary amount of water added to dilute it, then x = the percentage of Hb in the blood to be investigated—

$$w = \frac{k(w+b)}{b}.$$

It is very convenient to add a drop of caustic potash to blood and then to saturate it with CO.

[(d) The **Hæmoglobinometer** of Gowers is used for the clinical estimation of hæmoglobin (fig. 20). "The tint of the dilution of a given volume of blood with distilled water is taken as the index of the amount of hæmoglobin. The distilled water rapidly dissolves out all the hæmoglobin, as is shown by the fact that the tint of the dilution undergoes no change on standing. The colour of a dilution of average normal blood (one hundred times) is taken as the standard. The quantity of hæmoglobin is indicated by the amount of distilled water needed to obtain the tint with the same volume of blood under examination as was taken of the standard. On account of the instability of a standard dilution of blood, tinted glycerine-jelly is employed instead. This is perfectly stable, and by means of earmine and picro-carmin the exact tint of diluted blood can be obtained. The apparatus consists of two glass tubes of exactly the same size. One contains (D) a standard of the tint of a dilution of 20 cubic mm. of blood, in 2 cubic centimetres of water (1 in 100). The second tube (C) is graduated 100 degrees = 2 centimetres (100 times 20 cubic millimetres). The 20 cubic millimetres of blood are measured by a capillary pipette (B). This quantity of the blood to be tested is ejected into the bottom of the tube, a few drops of distilled water being first placed in the latter. The mixture is rapidly agitated to prevent the coagulation of the blood. The distilled water is then added drop by drop (from the pipette stopper of a bottle (A) supplied for that purpose), until the tint of the dilution is the same as that of the standard, and the amount of water which has been added (*i.e.*, the degree of dilution) indicates the amount of hæmoglobin."

"Since average normal blood yields the tint of the standard at 100 degrees of dilution, the number of degrees of dilution necessary to obtain the same tint with a given specimen of blood is the percentage proportion of the hæmoglobin contained in it, compared to the normal. For instance, the 20 cubic millimetres of blood from a patient with anæmia gave the standard tint of 30 degrees of dilution. Hence it contained only 30 per cent. of the normal quantity of hæmoglobin. By ascertaining with the hæmacytometer the corpuscular richness of the blood, we are able to compare the two. A fraction, of which the numerator is the percentage of hæmoglobin, and the denominator the percentage of corpuscles, gives at once the average value per corpuscle. Thus the blood mentioned above containing 30 per cent. of hæmoglobin, contained 60 per cent. of corpuscles; hence the average value of each corpuscle was $\frac{30}{60}$ or $\frac{1}{2}$ of the normal. Variations in the amount of hæmoglobin may be recorded on the same chart as that employed for the corpuscles. The instrument is only expected to yield approximate results, accurate within 2 or 3 per cent. It has, however, been found of much utility in clinical observation."

(e) **Fleischl's Hæmometer**.—For clinical purposes this instrument (fig. 21) is useful. A cylinder G, of two compartments a and a' rests on a metallic table. Both compartments are filled with water, but in one (a) is placed a known quantity of blood measured in a measuring-tube of known capacity. The red colour of the solution of hæmoglobin thus obtained is compared with a red wedge of glass (K), which is moved by means of a wheel (R and T) under the other compartment (a') until the two colours are identical. The illumination of the dilute blood solution and the red glass wedge is done from below by lamp light reflected from the white reflecting surface (S). The frame in which the red glass wedge is fixed bears numbers,

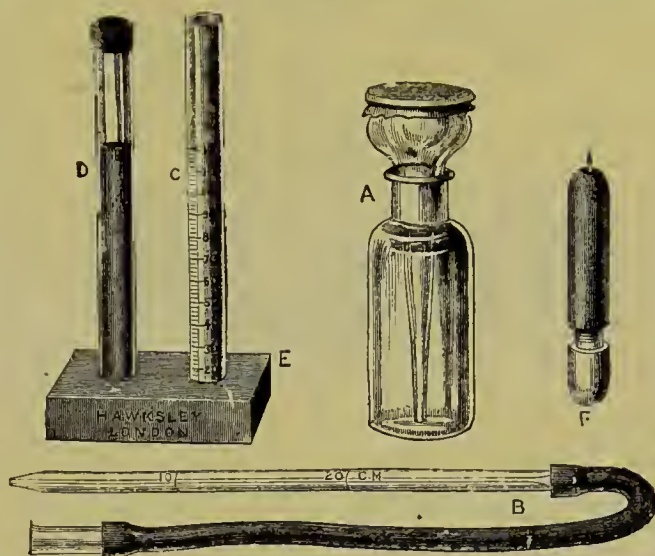


Fig. 20.

Gowers' hæmoglobinometer. A, pipette bottle for distilled water; B, capillary pipette; C, graduated tube; D, tube with standard dilution; F, lancet for pricking the finger.

and when the colour is identical in the two compartments *a* and *a'*, the percentage of hæmoglobin as compared with normal blood can be read off directly. Suppose it to be 80 on the scale, then the blood examined contains 80 per cent. of the hæmoglobin of normal blood.

[Bizzozero's chromoeytometer is largely used in Italy for the same purpose.]

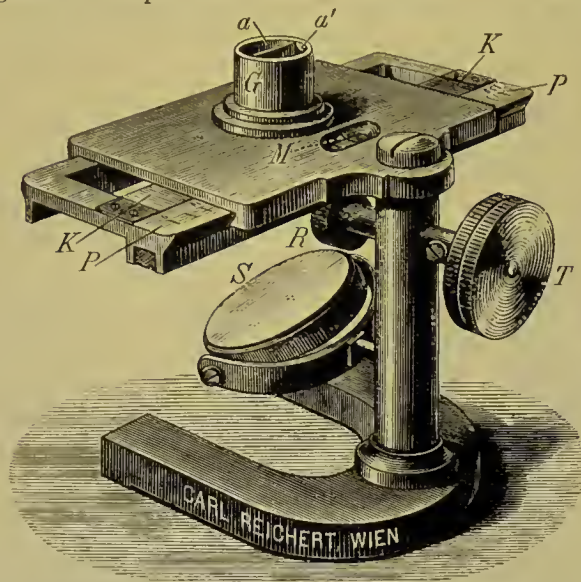


Fig. 21.

Fleisoh's hæmometer. *K*, red coloured wedge of glass moved by *R*; *G*, mixing vessel with two compartments *a* and *a'*; *M*, table with hole to read off the percentage of hæmoglobin on the scale *P*; *T*, to move *K*; *S*, mirror of plaster of Paris.

The amount of hæmoglobin in man is 13·77 per cent., in the woman 12·59 per cent., during pregnancy 9 to 12 per cent (*Preyer*). According to *Leichtenstern*, Hb is in greatest amount in the blood of a newly-born infant, but after ten weeks the excess disappears. Between six months and five years it is smallest in amount; it reaches its second highest maximum between twenty-one and forty-five, and then sinks again. From the tenth year onwards, the blood of the female is poorer in Hb. The taking of food causes a temporary decrease of the Hb owing to the dilution of the blood.

[In Animals.—The quantity of blood varies with the animal investigated. The following Table by *Beauvis* gives the proportion of hæmoglobin per 100 gram. of blood:—

Man, ...	12·3 per 100.	Sheep, ...	11·2 per 100.
Dog, ...	13·8 „	Rabbit, ...	8·4 „
Pig, ...	13·2 „	Fowl, ...	8·5 „
Ox, ...	12·3 „	Duck, ...	8·1 „

Pathological.—A decrease is observable during recovery from febrile conditions, and also during phthisis, cancer, ulcer of the stomach, cardiac disease, chronic diseases, chlorosis, leukemia, pernicious anemia, and during the rapid mercurial treatment of syphilitic persons. During hunger the Hb seems to be more resistant than the other constituents of the blood (*Groll*).

14. THE SPECTROSCOPE.—As the spectroscope is frequently used in the investigation of blood and other substances, a short description of the instrument is given here (fig. 22). It consists of—(1) a tube, *A*, which has at its peripheral end a slit, *S* (that can be narrowed or widened). At the other end a collecting lens, *C* (called a **collimator**), is placed, so that its focus is in exact line with the slit. Light (from the sun or a lamp) passes through the slit, and thus goes parallel through *C* to—(2) the prism, *P*, which decomposes the parallel rays into a coloured spectrum, *r, v*. (3) An astronomical telescope is directed to the spectrum *r, v*, and the observer, *B*, with the aid of the telescope, sees the spectrum magnified from six to eight times. (4) A third tube, *D*, contains a delicate scale, *M*, on glass, whose image, when illuminated, is reflected from the prism to the eye of the observer, so that he sees the spectrum, and over or above it the scale. To keep out other rays of light the inner ends of the three tubes are covered by metal or by a black cloth (see also § 265).

[The **micro-spectroscope**, *e.g.*, as made by *Browning* or *Zeiss*, may be used when small quantities of a solution are to be examined. Every spectroscope ought to give two spectra, so that the position of any absorption-band may be definitely ascertained. The spectroscope is fitted into the ocular end of the tube of a microscope instead of the eye-piece. Small cells for containing the fluid to be examined are made from short pieces of barometer-tubes cemented to a plate of glass.]

Absorption Spectra.—If a coloured medium (*e.g.*, a solution of blood) be placed between the slit and a source of light, all the rays of coloured light do not pass through it—some are absorbed; many yellow rays are absorbed by blood, hence that part of the spectrum appears

dark to the observer. On account of this absorption, such a spectrum is called an "*absorption spectrum*."

Flame Spectra.—If mineral substances be burned on a platinum-wire in a *non-luminous* flame or Bunsen's burner in front of the slit, the elements present in the mineral or ash give a special coloured band or bands, which have a definite position. Sodium gives a yellow, potassium a red and violet line. These substances are found on burning the ashes of almost all organs.

If sunlight be allowed to fall upon the slit, the spectrum shows a large number of lines (*Fraunhofer's lines*) which occupy definite positions in the coloured spectrum. These lines are indicated by the letters A, B, C, D, &c., *a, b, c, &c.* (fig. 23).

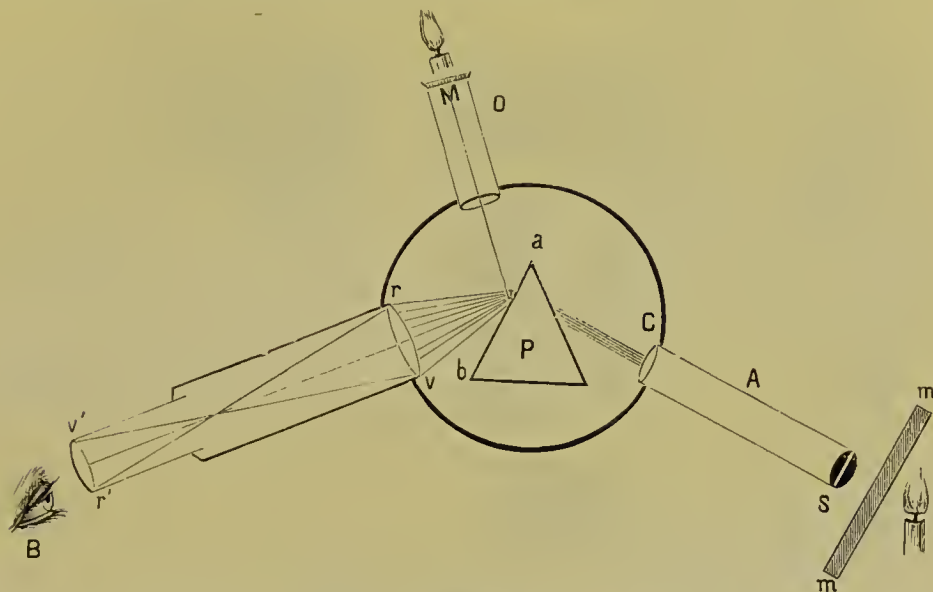


Fig. 22.

Scheme of a spectroscope for observing the spectrum of blood. A, tube; S, slit; *m, m*, layer of blood with flame in front of it; P, prism; M, scale; B, eye of observer looking through a telescope; *r, v*, spectrum.

15. COMPOUNDS OF HB WITH O; OXYHÆMOGLOBIN AND METHÆMOGLOBIN.—1. **Oxyhæmoglobin** (HbO_2) behaves as a weak acid, and occurs to the extent of 86·78 to 94·30 per cent. in dry human red corpuscles (*Jüdel*). It is formed very readily whenever Hb comes into contact with O or atmospheric air. According to Bohr, 1 gramme Hb unites with 1·56 cubic centimetre of O at 0° and 760 mm. Hg pressure, the union being stronger in weak than in concentrated solutions. Oxyhæmoglobin is a very **loose chemical compound**, and is slightly less soluble than Hb; its **spectrum** shows in the *yellow* and the *green two dark absorption-bands*, whose length and breadth in a 0·18 per cent. solution are given in fig. 23 (2). It occurs in the blood-corpuscles circulating in arteries and capillaries, as can be shown by the spectroscopic examination of the ear of a rabbit, of the prepuce, and the web of the fingers (*Vierordt*).

[**Spectrum of Oxyhæmoglobin.**—In the spectrum of a dilute solution of hæmoglobin crystals or arterial blood, part of the red and violet rays are absorbed, but **two** well-marked **absorption-bands** exist between D and E. The line nearest D, *i.e.*, next the red end of the spectrum, sometimes designated by the letter (*a*) is narrow, sharply defined, and black at its centre, and its position corresponds to the wave-length 579. The other absorption-band near E, conveniently designated by (*β*), is broader, not so dark, and its edges are less sharply defined. Its centre corresponds to the wave-length 553·8. In very dilute solutions the *a* band is the only one visible. In a strong solution, as shown in fig. 23, the two bands fuse, but are again made visible as two on dilution of the blood.]

[The spectrum necessarily varies with the concentration of the solution. Fig. 24 shows how the absorption-bands increase with increase in the strength of the solution. With a 1 per cent. solution all the spectrum disappears, with the exception of the extreme red, and as the dilution continues we see successively the orange, green, yellow, blue, indigo, and violet. With .65 per cent. of HbO_2 there is only one absorption-band.]

Reduction of Oxyhæmoglobin.—It gives up its O very readily, however, even

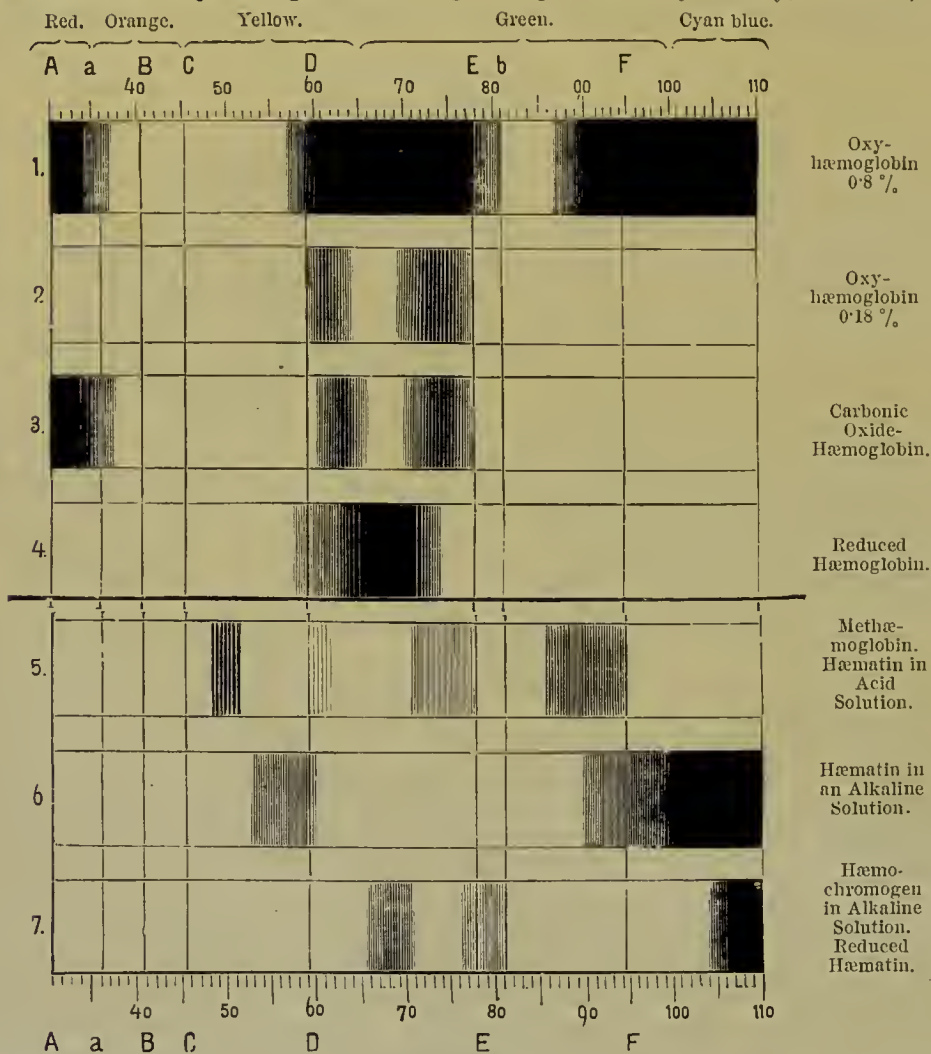


Fig. 23.

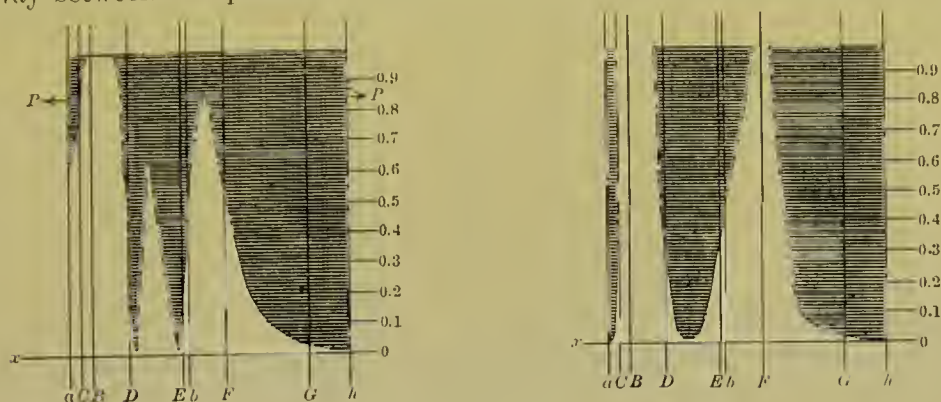
Spectra of hæmoglobin and its compounds.

when means which set free absorbed gases are used. It is **reduced** (1) by the removal of the gases by the *air-pump*, (2) by the *conduction* through its solution of *other gases* (CO), and (3), by *heating* to the boiling-point. In the circulating blood its O is very rapidly given up to the tissues, so that in suffocated animals only *reduced hæmoglobin* is found in the arteries. Some constituents of the serum and sugar remove its O.

Spectrum of reduced Hæmoglobin.—By adding to a solution of oxyhæmoglobin **reducing substances**—*e.g.*, ammonium sulphide, iron filings, or Stokes's fluid [tartaric acid, iron proto-sulphate, and excess of ammonia]—the two absorption-bands of the spectrum disappear, and **reduced hæmoglobin** (gas free), with **one**

absorption-band, is formed. The colour changes from a bright red to a purplish or claret tint. The two bands are reproduced by shaking the reduced hæmoglobin with air, whereby HbO_2 is again formed. Solutions of oxyhæmoglobin are readily distinguished by their scarlet colour from the purplish tint of reduced hæmoglobin.

[The single absorption-band (fig. 23, 4), designated by the letter (γ), lying about midway between the position of the two previous bands, is broader, fainter, less



Figs. 24 and 25.

Fig. 24, graphic representation of the spectrum of HbO_2 . Fig. 25, the same of Hb , showing the amount of absorption with varying strengths of hæmoglobin, the thickness of the fluid remaining the same. The numbers indicate the percentage of colouring matter.

deeply shaded, and its centre is about, but not quite, intermediate between D and E. It extends between the wave-lengths 595 and 538, and is blackest opposite the wave-length 550, so that it lies nearer D than E. At the same time more of the blue rays are transmitted. On dilution the band is not resolved into two, but simply becomes fainter and disappears.]

[According to Hermann, the absorption-band of Hb is not a single band, there being in addition a very narrow band towards the red end of the spectrum, but separate from the chief absorption-band by a very small interval.]

[Hæmoglobin has certain remarkable characters:—(1) Although it is a crystalloid body it diffuses with difficulty through an animal membrane, owing to the large size of its molecule. (2) It readily combines with O to form an unstable and loose chemical compound, oxyhæmoglobin. (3) This O it gives up readily to the tissues or other deoxidising reagents. (4) Its composition is very complex, for, in addition to the ordinary elements present in proteids, it contains a remarkable amount of iron (0.4 per cent).]

If a string be tied round the base of two fingers so as to interrupt the circulation, spectroscopic examination shows that the oxyhæmoglobin rapidly passes into reduced Hb (*Vierordt*). Cold delays this reduction; it is accelerated in youth, during muscular activity, or by suppressed respiration, and usually also during fever.

The spectroscopic examination of small blood-stains is often of the utmost forensic importance. A minimal drop is sufficient. Dissolve the stain in a few drops of distilled water, and place the solution in a thin glass tube in front of the slit of the spectroscope.

Para-hæmoglobin.—If HbO_2 be preserved under alcohol it passes into a modified form, which is insoluble in water (*Nencki and Sieber*).

2. Methæmoglobin is a more stable, crystalline compound (*Hoppe-Seyler*). It contains the same amount of O as HbO_2 , but in a different chemical union, while the O is also more firmly united with it. It shows **four absorption-bands** like hæmatin in acid solution (fig. 23, 5), of which that between C and D is distinct; the second is very indistinct, while the third and fourth readily fuse, so that these last two bands are only well seen with good apparatus.

It is produced spontaneously in old brown blood-stains, in the crusts of bloody wounds, in cysts with sanguinolent contents, and in bloody urine. Chemically, it can be prepared from

a solution of Hb by the action of potassic ferrieyanide (*Jüderholm*) or potassic ehlorate (*Marchand*), [or by adding to a solution of Hb a frèshly-prepared solution of potassic permanganate, by nitro-benzol, azobenzol, kairin, sodium nitrite, pyrogallie acid]; and in non-laky blood by alloxantin (*Kowalewsky*). It erySTALLISES if defibrinated blood is shaken with amyl nitrite and the mahogany-brown laky fluid be allowed to evaporate slowly (*Halliburton*).

If a trace of ammonia be added to a solution of methæmoglobin, it gives an alkaline solution of methæmoglobin, which shows two bands like oxyhæmoglobin, of which the first one is the broader, and extends more towards the red. If ammonium sulphide be added to the methæmoglobin solution, reduced Hb is formed.

[Action of Nitrites.]—The addition of amyl nitrite dissolved in alcohol, or sodie or potassic nitrite to defibrinated blood causes the latter to assume a chocolate colour, which, on the addition of ammonia, changes to red. The chocolate-coloured fluid shows one well-defined band in the red, and less distinctly other three bands like methæmoglobin (*Gamgee*).]

[The nitrites therefore form a compound with its oxygen more firmly fixed than the O in HbO_2 , so that large doses of nitrites arrest the internal respiration and are poisonous. It is, however, affected by the products formed in the blood during asphyxia, while CO-Hb is not, the methæmoglobin formed by the nitrites is reduced by these products to Hb, which as it passes through the lungs takes up O.]

16. CARBONIC OXIDE-HÆMOGLOBIN, POISONING WITH CO.—3. CO-Hæmoglobin is a more stable chemical compound than the foregoing, and is produced at once when earbonie oxide is brought into contact with pure Hb or HbO_2 (*Cl. Bernard*, 1857). It has an intensely florid or *cherry-red* colour, is not dichroic, and its spectrum shows **two absorption-bands**, very like those of HbO_2 , but they are slightly closer together and lie more towards the violet (fig. 23, 3). Redueing substances which act upon HbO_2 , *e.g.*, ammonium sulphide or Stokes's fluid, do not affect these bands, *i.e.*, they cannot convert the CO-Hb into reduced Hb. If a 10 per cent. solution of caustie soda be added to a solution of CO-Hb, and heated, it gives a *cinnabar-red* colour; while, with an HbO_2 solution, it gives a dark brown, greenish, greasy mass. Spectrum analysis and the soda test enable one to distinguish $\frac{3}{10}$ HbCO, mixed with $\frac{7}{10}$ HbO_2 . Oxidising substances [solutions of potassic permanganate (0.025 per cent.), potassic ehlorate (5 per cent.), and dilute chlorine solution] make solutions of CO-Hb cherry-red in colour, while they turn solutions of HbO_2 pale yellow. After this treatment both solutions show the absorption-bands of methæmoglobin, but those of the CO-Hb appear considerably later. If ammonium sulphide be added, HbO_2 and CO-Hb are re-formed.

Hb-CO Reactions.—*Modified Soda Test.*—Dilute the blood 20 times and add an equal volume of caustie soda (S. G. 1340) (*Salkowski*). [Dilute 1 c.cm. HbCO with 50 c.cm. of water, to 10 c.cm. of this mixture add 0.2 c.cm. orange-coloured ammonium sulphide (2 grms. of sulphur are added to 100 c.cm. yellow ammonium sulphide), and then 0.2 c.cm. of 30 per cent. acetic acid. The HbCO blood becomes bright red, while normal blood becomes greenish-gray (*Katayama*).]

On account of its **stability**, CO-Hb resists external influences and even putrefaction for a long time, and the two bands of the spectrum may be visible after many months. Landois obtained the soda test and spectroscopic bands in the blood of a woman poisoned eighteen months previously by CO, and after great putrefaction of the body had taken place. [Stirling has kept CO-Hb in a stoppered bottle for five years without putrefaction taking place.]

If CO or air containing it be inspired, it gradually displaces the O, volume for volume, out of the red blood-corpuscles, and death soon occurs; 1000 c.cm. inspired at once will kill a man. A very small quantity in the air ($\frac{1}{4000} - \frac{1}{10000}$) suffices, in a relatively short time, to form a large quantity of CO-Hb. As continued contact with other gases (such as the passing of O through it for a very long time) gradually separates the CO from the Hb, with the formation of HbO_2 , it happens that, in very partial poisoning with CO, the blood gradually gets rid of the CO by the respiratory organs. It does not appear that any part is further oxidised into CO_2 in the organism. [CO-hæmoglobin, being a stable compound when once formed, circulates in the blood-vessels; but it neither gives up oxygen to the tissues, nor takes up oxygen in the lungs, hence its very poisonous properties.]

The real cause of death in animals poisoned with it is, that the internal respiration is arrested.]

Poisoning with Carbonic Oxide.—Carbonic oxide is formed during the incomplete combustion of coal or coke, and passes into the air of the room, provided there is not a free outlet for the products of combustion. It occurs to the extent of 12–28 per cent. in ordinary gas, which largely owes its poisonous properties to the presence of CO. If the O be gradually displaced from the blood by the respiration of air containing CO, life can only be maintained as long as sufficient O can be obtained from the blood to support the oxidations necessary for life. Death occurs before all the O is displaced from the blood. CO has no effect when directly applied to muscle and nerve. When it is mixed with air, as in **coal-gas poisoning**, and inhaled, there is first stimulation and afterwards paralysis of the nervous system, as shown by the symptoms induced, *e.g.*, violent headache, great restlessness, excitement, increased activity of the heart and respiration, salivation, tremors, and spasms. Later, unconsciousness, weakness, and paralysis occur, laboured respiration, diminished heart-beat, and lastly, complete loss of sensibility, cessation of the respiration and heart-beat, and death. At first the temperature rises several tenths of a degree, but it soon falls 1° or more. The pulse is also increased at first, but afterwards it becomes very small and frequent. In poisoning with pure CO there is no dyspnoea, but sometimes muscular spasms occur, the coma not being very marked. There is also temporary but pronounced paralysis of the limbs, followed by violent spasms. After death the heart and brain are congested with intensely florid blood. In poisoning with the **vapour of charcoal**, where CO and CO₂ both occur, there is a varying degree of coma; pronounced dyspnoea, muscular spasms which may last several minutes, gradual paralysis and asphyxia, moniliform contractions and subsequent dilatation of the blood-vessels, with congestion of various organs, occur, accompanied by a fall of the blood-pressure (*Klebs*), indicating initial stimulation and subsequent paralysis of the vaso-motor centre. This also explains the variations in the temperature and the occasional occurrence of sugar in the urine after poisoning with CO. After death, the blood-vessels are found to be filled with fluid blood of an exquisitely bright cherry-red colour, while all the muscles and viscera and exposed parts of the body (such as the lips) have the same colour. The brain is soft and friable; there is catarrh of the respiratory organs and degeneration of the muscles, and great congestion and degeneration of the liver, kidneys, and spleen. The spots of lividity, *post-mortem*, are bright red. After recovery from poisoning with CO there may be paraplegia and (although more rarely) disturbances of the cerebral activity.

17. OTHER COMPOUNDS OF HÆMOGLOBIN—4. **Nitric Oxide-Hæmoglobin (NO-Hb)** is formed when NO is brought into contact with Hb (*L. Hermann*).

As NO has a great affinity for O, red fumes of nitrogen peroxide (NO₂) being formed whenever the two gases meet, it is clear that, in order to prepare NO-Hb, the O must first be removed. This may be done by passing H through it, [or ammonia may be added to the blood, and a stream of NO passed through it; the ammonia combines with all the acid formed by the union of the NO with the O of the blood]. NO-Hb is a *more stable chemical compound* than CO-Hb, which, as we have seen, is again more stable than HbO₂. It has a *bluish-violet* tint, and also gives two absorption-bands in the spectrum similar to those of the other two compounds, but not so intense. These bands are *not* abolished by the action of reducing agents. As NO-Hb cannot be formed in the body, it has no practical significance.

The three compounds of Hb, with O, CO, and NO, are **crystalline**, like reduced Hb; they are **isomorphous**, and their solutions are **not dichroic**. All three gases unite in equal volumes with Hb. If O be conducted through a concentrated solution of Hb devoid of gases, a crystalline mass of HbO₂ is thereby readily formed.

5. **Cyanogen**, CNH (*Hoppe-Seyler*), and **acetylene**, C₂H₄ (*Bristow and Liebreich*), form easily decomposable compounds with Hb. The former occurs in poisoning with hydrocyanic acid, and has a spectrum nearly identical with that of HbO₂, and, like HbO₂, it is reduced, but very slowly, by special reagents. [The existence of these compounds is, however, highly doubtful (*Gamgee*).]

18. DECOMPOSITION OF HÆMOGLOBIN.—In solution and in the dry state Hb gradually becomes decomposed, whereby the iron-containing pigment hæmatin (along with certain bye-products, formic, lactic, and butyric acids), is formed. Hæmoglobin, however, may be decomposed at once into—(1) **Hæmatin**, a body containing iron, and (2) a colourless proteid closely related to **globulin**; by

(a) the addition of all acids, even by CO_2 in the presence of plenty of water; (b) strong alkalies; (c) all reagents which coagulate albumin, and by heat at $70^\circ - 80^\circ \text{C.}$; (d) by ozone.

(A) **Hæmatin**, $\text{C}_{32}\text{H}_{32}\text{N}_4\text{FeO}_4$ (*Nencki and Sieber*), is a bluish-black amorphous body, which forms about 4 per cent. of hæmoglobin (dog). It is *insoluble* in water, alcohol, and ether; *soluble* in dilute alkalies and acids, and in acidulated ether and alcohol.

(1) **Acid Hæmatin**.—Lecanu extracted it from dry blood-corpuscles by using alcohol containing sulphuric and tartaric acids. [If acetic acid be added to a solution of Hb and slightly heated, a mahogany-brown fluid is obtained, containing *hæmatin in acid solution*, which gives a spectrum with **one absorption-band** to the red side of D near C (fig. 23, 5). There is at the same time a considerable absorption of the blue end of the spectrum. If an **ethereal extract** of the acid-hæmatin be made, the ether is coloured brown and shows **four absorption-bands**, as in fig. 23, 5.]

(2) **Alkali-hæmatin**.—[If to the above solution ammonia or caustic soda be added, on heating gently, the colour changes and the fluid becomes dichroic, showing a greenish tinge. On mixing the solution thoroughly with air the spectrum of oxy-alkali-hæmatin is obtained, *i.e.*, **one absorption-band** just to the red side of D (fig. 23, 6), so that it is much nearer D than the corresponding band of acid-hæmatin. Much of the blue end of the spectrum is absorbed as well.]

[(3) **Reduced Alkali-hæmatin** or **Hæmochromogen**.—If the solution of alkali-hæmatin be reduced by ammonium sulphide, the spectrum of hæmochromogen is obtained, *viz.*, **two absorption-bands** between D and E, but they are nearer the violet end than in the case of HbO_2 and Hb-CO (fig. 23, 7).]

[(4) **Hæmatoporphyrin** or **Iron-free Hæmatin**.—On adding blood to concentrated sulphuric acid a clear purplish-red solution is obtained, which shows **two absorption-bands**, one close to and on the red side of D, and a second half-way between D and E. If water be added a brown precipitate is thrown down. When this precipitate is dissolved in caustic soda, it gives a fluid which shows *four* absorption-bands.]

Action of CO_2 .—If CO_2 be passed through a solution of oxyhæmoglobin for a considerable time, reduced Hb is first formed; but if the process be prolonged the Hb is decomposed, a precipitate of globulin is thrown down, and an absorption-band, similar to that obtained when Hb is decomposed with acids, is observed (p. 30).

An alkaline solution of hæmatin, when reduced by tin and hydrochloric acid, yields **urobilin** (compare § 261).

When hæmoglobin is extravasated into the subcutaneous tissue, it becomes so altered that at first hæmatoidin (§ 20), and ultimately hydrated oxide of iron, appear in its place.

19. HÆMIN AND BLOOD TESTS.—In 1853 Teichmann prepared crystals of hæmin from blood, which Hoppe-Seyler showed to be **chloride of hæmatin** (Hæmatin, + 2HCl), with the formula $\text{C}_{32}\text{H}_{31}\text{ClN}_4\text{FeO}_3$ (*Nencki and Sieber*). The presence of these crystals is used as a test for blood-stains or blood in solution. They (fig. 26) are prepared by adding a small crystal of common salt to dry blood on a glass slide, and then an excess of *glacial* acetic acid; the whole is gently heated until bubbles of gas are given off. On allowing the preparation to cool, the characteristic hæmin crystals are obtained.

Characters.—When well formed, the crystals are small microscopic rhombic plates, or rods; sometimes they are single—at other times they are aggregated in groups, often crossing each other (fig. 26). Some kinds of blood (ox and pig) yield very irregular, scarcely crystalline, masses. The crystalline forms of hæmin are identical in all the different kinds of blood that have been examined. They are **doubly refractive**; under the polarization microscope they are a glancing

yellow, appearing raised on the dark field, with a strong absorption of the light parallel to the long axis of the crystals (*Falk and Morache*). They are **pleo-chromatic**: by transmitted light they are mahogany-brown, and by reflected light bluish-black, glancing like steel.

(1) **Preparation from Dry Blood-Stains.**—Place a few particles of the blood-stain on a glass slide, add 2 to 3 drops of *glacial* acetic acid and a small crystal of common salt; cover with a cover-glass, and heat gently over the flame of a spirit-lamp until bubbles of gas are given off. On cooling, the crystals appear in the preparation (fig. 26).

(2) **From Stains on Porous Bodies.**—The stained object (cloth, wood, blotting-paper, earth) is extracted with a small quantity of dilute caustic potash, and afterwards with water in a watch-glass. Both solutions are carefully filtered, and tannic acid and glacial acetic acid are added until an acid reaction is obtained. The dark precipitate which is formed is collected on a filter and washed. A small part of it is placed on a microscope slide, a granule of common salt is added, and the whole dried; the dry stain is treated as in (1) (*Struwe*).



Fig. 26.

Hæmin crystals. 1, human; 2, seal; 3, calf; 4, pig; 5, lamb; 6, pike; 7, rabbit.

(3) **From Fluid Blood.**—Dry the blood slowly at a low temperature, and proceed as in (1).

(4) **From Dilute Solutions of Hæmoglobin.**—(a) *Struwe's Method.*—Add to the fluid, ammonia, tannic acid, and afterwards glacial acetic acid, until it is acid; a black precipitate of tannate of hæmatin is thrown down. This is isolated, washed, dried, and treated as in (1), but instead of NaCl a granule of ammonium chloride is added.

Hæmin crystals may sometimes be prepared from putrefying or lake-coloured blood, but they are very small, and the test often fails. When mixed with iron-rust, as on iron weapons, the blood-crystals are generally not formed. In such cases, scrape off the stains and boil them with dilute caustic potash. If blood be present, the dissolved hæmatin forms a fluid, which in a thin layer is green, in a thick layer red (*H. Rose*).

Hæmin crystals have been prepared from all classes of vertebrates and from the blood of the earth-worm. From the blood of the ox and pig they may be almost amorphous.

Chemical Characters.—They are insoluble in water, alcohol, ether, chloroform; but concentrated H_2SO_4 dissolves them, expelling the HCl, and giving a violet-red colour. Ammonia also dissolves them, and if the resulting solution be evaporated, heated to 130°C ., and treated with boiling water (which extracts the ammonium chloride), **hæmatoporphyrin**—identical with Mulder's iron-free hæmatoin, and with Preyer's hæmatoin, is obtained (*Hoppe-Seyler*). It is a bluish-black substance, which on being pounded forms a brown and amorphous powder. Its solutions in caustic alkalies are dichroic: in reflected light brownish-red; in transmitted light, in a thick stratum, red—in a thin one, olive-green. The acid solutions are monochromatic and brown.

Preparation in Bulk.—To obtain it in quantity, heat dried horse's blood with 10 parts of formic acid. If the crystals be suspended in methyl alcohol, on adding iodine and heating them they dissolve with a purple colour; after adding bromine, brown; and after passing chlorine gas, green; all these give a characteristic spectrum (*Axenfeld*).

The glacial acetic acid may be replaced by oxalic or tartaric acid, the common salt by salts of iodine or bromine; in the latter case similar bromine- or iodine-hæmatin is formed (*Bikfalvi*).

20. HÆMATOIDIN.—Virehow discovered this important derivative in hæmoglobin. It occurs in the body wherever blood stagnates outside the circulation, and becomes decomposed—as when blood is extravasated into the tissues—*e.g.*, the brain—in solidified blood-plugs or thrombi, especially in veins; invariably in the Graafian follicles. It contains no iron ($\text{C}_{32}\text{H}_{30}\text{N}_4\text{O}_6$), and crystallises in clino-rhombic prisms (fig. 27) of a yellowish-brown colour. It is soluble in warm alkalies and chloroform. Very probably it is identical with the bile-pigment—**bilirubin**. [When acted upon by impure nitric acid (*Gmelin's reaction*), it gives the same play of colours as bile.]

Pathological.—In cases where a large amount of blood has undergone solution within the blood-vessels (as by injecting foreign blood) hæmatoidin crystals have been found in the urine. For their occurrence in the urine in jaundice (§ 180), and in the sputum (§ 138).

21. (B.) THE COLOURLESS PROTEID OF HÆMOGLOBIN.—It is closely related to globulin; but while the latter is precipitated by all acids, even by CO_2 , and re-dissolved on passing O through it, the proteid of hæmoglobin, on the other hand, is not dissolved after precipitation on passing through it a stream of O.



Fig. 27.

Hæmatoidin crystals.

As crystals of hæmoglobin can be decolorised under special circumstances, it is probable that these owe their crystalline form to the proteid which they contain. Landois placed crystals of hæmoglobin along with alcohol in a dialyser, putting ether acidulated with sulphuric acid outside, and thereby obtained colourless crystals. [If frogs' blood be sealed up on a microscopic slide along with a few drops of water for several days, long colourless acicular crystals are developed in it (*Stirling and Brito*).]

22. II. PROTEIDS OF THE STROMA.—Dry red human blood-corpuscles contain from 5·10–12·24 per cent. of these proteids, but little is known about them (*Jüdel*). One of them is globulin, which is combined with a body resembling nuclein (*Woodbridge*), and traces of a diastatic ferment (*v. Wittich*). The stroma tends to form masses which resemble fibrin.

L. Brunton found a body resembling mucin in the nuclei of red blood-corpuscles, and Miescher detected nuclein (§ 250, 2).

[**Stromata of the Red Corpuscles.**—When mammalian red blood-corpuscles are treated with water—or other reagents, such as dilute acids, ether, &c.—the 80 or 90 per cent. of hæmoglobin which they contain is dissolved out from the corpuscles, and the colourless less soluble part which remains is called the “stroma.” The stromata retain somewhat the shape of the original corpuscles, and are composed of proteid, lecithin, cholesterin, and inorganic salts (chiefly potassium phosphate.)]

[The stromata are obtained by treating defibrinated blood with a very large volume of 1 per cent. sodic chloride. The proteids can be extracted from the stromata with various saline media, *e.g.*, Na_2SO_4 (half-saturated), NaCl (5 per cent.), MgSO_4 (5 per cent.).]

The saline extract contains abundance of what Halliburton calls cell-globulin—a globulin that in heat-coagulation temperature, precipitability by salts and other reagents, and in ferment activity resembles the proteid called cell-globulin derived from lymph-cells or white blood-corpuscles (p. 33), so that stroma-globulin and cell-globulin are probably identical. Cell-Albumin is either absent or only present in minute traces, nor does nuclein or nucleo-albumin appear to be present, while the albumoses and peptones are certainly absent.]

[The proteid cell-globulin has fibrino-plastic properties, *i.e.*, it can cause the formation of fibrin to take place in a suitable fluid, *e.g.*, hydrocele and pericardial fluid, but it is not decided whether the cell-globulin and fibrin-ferment are identical, or merely in close relationship with one another, the balance of evidence, however, being in favour of the former view (*Halliburton*).]

There is thus seen to be a very great difference between the proteids of the coloured and the colourless corpuscles (p. 33), a matter of some importance in connection with the views one may hold regarding the true cellular nature of the coloured corpuscles.]

23. OTHER CONSTITUENTS OF RED BLOOD-CORPUSCLES.—III. **Lecithin** (0·35–0·72 per cent.) in dry blood-corpuscles (§ 250, 2). **Cholesterin** (0·25 per cent.) (§ 250, III.), **no Fats**.

Lecithin is regarded as a glycerin-phosphate of neurin, in which, in the radical of glycerin-phosphoric acid, two atoms of H are replaced by two molecules of the radical of stearic acid. By gentle heat glycerin-phosphoric acid is split up into glycerine and phosphoric acid (§ 250).

These substances are obtained by extracting old stromata or isolated blood-corpuscles with ether. When the ether evaporates, the characteristic globular forms (“myelin-forms”) of lecithin and crystals of cholesterin are recognised. The amount of lecithin may be determined from the amount of phosphorus in the ethereal extract.

IV. Water (681·63 per 1000—*C. Schmidt*).

V. Salts (7·28 per 1000), chiefly compounds of potash and phosphoric acid; the phosphoric acid is derived only from the burned lecithin; while the greater part of the sulphuric acid is derived from the burning of the hæmoglobin in the analysis.

Analysis of Blood.—1000 parts, by weight, of horse's blood contain :—

344·18 blood-corpuscles (containing about 128 per cent. of solids).

655·82 plasma (containing about 10 per cent. of solids).

1000 parts, by weight, of moist blood-corpuscles contain :—

Solids, ... 367·9 (pig) ; 400·1 (ox).

Water, ... 632·1 „ 599·9 „

The solids are :—

	Pig.	Ox.
Hæmoglobin, ...	261	280·5
Proteids, ...	86·1	107
Lecithin, Cholesterin, and other Organic Bodies,	12·0	7·5
Inorganic salts, ...	8·9	4·8
Including { Potash, ...	5·543	0·747
{ Magnesia, ...	0·158	0·017
{ Chlorine, ...	1·504	1·635
{ Phosphoric Acid, ...	2·067	0·703
{ Soda, ...	0	2·093 (<i>Bunge</i>).

[An approximate estimate of the composition of human blood is given in the following table :—

Composition of Human Blood as a Whole.

Water, ...	780
Solids—of these—	
Hæmoglobin, ...	134
Serum-albumin, ...	70
Serum-globulin, }	2·2
Fibrin of Clot (? Fibrinogen), ...	6·0
Inorganic Salts (of serum), ...	6·2
Extractives, ...	1·4
Fatty matters, ...	

Gases, O, CO₂, N.]

Moist red blood-corpuscles contain 30–40 per cent. of solids and 70–60 per cent. of water. Of the *dry solids* of the red corpuscles at least 90 per cent. is hæmoglobin, 8 proteid matter, and 2 other substances.]

24. CHEMICAL COMPOSITION OF THE WHITE CORPUSCLES.—Investigations have been made on pus cells (*Miescher*), which closely resemble colourless blood-corpuscles. They contain several **proteids**; alkali-albuminate, a proteid which coagulates at 48° C., an albuminate resembling myosin, paraglobulin, peptone, and a coagulating ferment; **nuclein** in the nuclei (§ 250, 2), glycogen (§ 252), lecithin, cerebrin, cholesterin, and fat.

100 parts, by weight, of dry pus contain the following Salts :—

Earthy Phosphates, ... 0·416	Potash, ... 0·201
Sodic Phosphate, ... 0·606	Sodic Chloride, ... 0·143

[**Proteids of the white corpuscles.**—Halliburton used the lymph-corpuscles of lymphatic glands, from which the proteids were dissolved out by a partially saturated solution of sodium sulphate. These cells contain :—

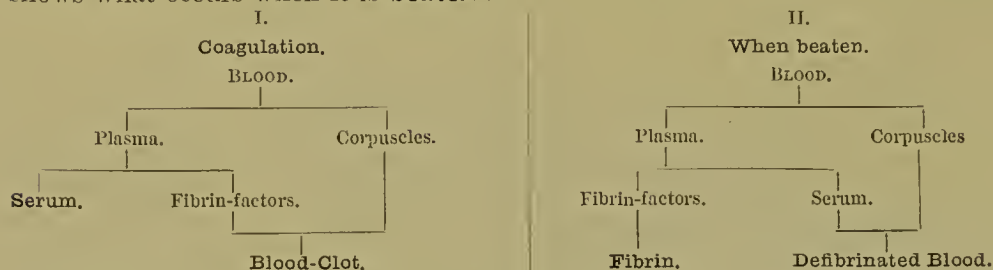
- (1) Cell-globulin α , in small quantity. It coagulates at 48°–50° C.
- (2) Cell-globulin β , in large quantity, and is either identical with or closely associated with the fibrin ferment. It coagulates in 5 per cent. MgSO₄ solution at 75° C.
- (3) Cell-albumin, which coagulates at 73° C.
- (4) Mucin-like body (*Miescher*), and called hyaline substance by Rovida. It is, however, not mucin, is rich in phosphorus, and yields nuclein on gastric digestion, in addition to albumoses and peptones, so that it belongs to the class of **nucleo-albumins**.
- (5) If the cells be not examined when they are quite fresh, they become acid from the formation of sarcolactic acid, and the proteolytic action of a ferment (pepsin?) found in the cell, comes into play with the subsequent formation of albumoses and peptones.

The foregoing list of proteids may be taken as those present in a typical cell and in protoplasm generally.]

25. BLOOD-PLASMA AND ITS RELATION TO SERUM.—The unaltered fluid in which the blood-corpuscles float is called **blood-plasma**, or **liquor sanguinis**. This fluid, however, after blood is withdrawn from the vessels, rapidly undergoes a change, owing to the formation of a solid fibrous substance—

fibrin. After this occurs, the new fluid which remains no longer coagulates spontaneously (it is plasma, *minus* the fibrin-factors), and is called **blood-serum**. Apart from the presence of the fibrin-factors, the chemical composition of plasma and serum is the same.

When **blood coagulates**, Table I. shows what takes place, while Table II. shows what occurs when it is **beaten** :—



Plasma is a clear, transparent, slightly thickish fluid, which, in most animals (rabbit, ox, cat, dog), is almost colourless; in man it is yellow, and in the horse citron yellow.

26. PREPARATION OF PLASMA.—(A) **Without Admixture.**—Taking advantage of the fact that plasma, when cooled to 0° outside the body, does not coagulate for a considerable time, Brücke prepares the plasma thus :—The blood of the horse (because it coagulates slowly, and its corpuscles sink rapidly to the bottom) is received, as it flows from an artery, into a tall narrow glass, placed in a freezing-mixture, and cooled to 0°. The blood remains fluid, the coloured corpuscles subside in a few hours, while the plasma remains above as a clear layer, which can be removed with a cooled pipette. If this plasma be then passed through a cooled filter, it is robbed of all its colourless corpuscles. [Burdon-Sanderson uses a vessel consisting of three concentric compartments—the outer and inner contain ice, while the blood is caught in the central compartment, which does not exceed half an inch in diameter.] The *quantity* of plasma may be roughly (but only roughly) estimated by using a tall, graduated measuring-glass. If the plasma be warmed, it soon coagulates (owing to the formation of the fibrin), and passes into a trembling jelly. If, however, it be beaten with a glass rod, the fibrin is obtained as a white stringy mass, adhering to the rod. The quantity of fibrin in a given volume of plasma is very small (p. 35), although it varies much in different cases.

(B) **With Admixture.**—Blood flowing from an artery is caught in a tall vessel containing $\frac{1}{4}$ th of its volume of a concentrated solution of sodic sulphate (*Hewson*)—or in a 25 per cent. solution of magnesian sulphate (1 vol. to 4 vols. blood—*Simmer*)—or 1 vol. blood with 2 vols. of a 4 per cent. solution of monophosphate of potash (*Masia*). When the blood is mixed with these fluids and put in a cool place, the corpuscles subside, and the clear stratum of plasma mixed with the salts may be removed with a pipette. [The plasma so obtained is called “**salted plasma**.”] If the salts be removed by dialysis, coagulation occurs; or it may be caused by the addition of water (*Joh. Müller*). Blood which is mixed with a 4 per cent. solution of common salt does not coagulate, so that it also may be used for the preparation of plasma. [For frog’s blood Johannes Müller used a $\frac{1}{2}$ per cent. solution of cane-sugar, which permits the corpuscles to be separated from the plasma by filtration. The plasma mixed with the sugar coagulates in a short time.]

27. COAGULATION OF THE BLOOD.—FIBRIN.—[Blood within the living body is fluid, and when first shed it remains so for a short time. After

a brief interval it becomes viscid, and then the whole mass becomes solid, clots, or **coagulates**, forming a complete jelly, so that at first the whole mass can be emptied out of the vessel in which it has set, and forms a mould having the shape of the vessel. The coagulation is due to the formation of a body called **fibrin**.]

General Characters.—**Fibrin** is that substance which, becoming solid in shed blood, in plasma and in lymph causes **coagulation** of these fluids. In these fluids, when left to themselves, fibrin is formed, consisting of innumerable, excessively delicate, closely-packed, microscopic, doubly refractive fibrils (fig. 9, E). These fibrils entangle the blood-corpuscles as in a spider's web, and form with them a jelly-like solid mass called the **blood-clot**, **crassamentum**, or **placenta sanguinis**. At first the clot is very soft, and after the first 2 to 15 minutes a few fibres may be found on its surface; these may be removed with a needle, while the interior of the clot is still fluid. The fibres ultimately extend throughout the entire mass, which, in this stage, has been called *cruor*. After from 12 to 15 hours the fibrin contracts, or at least shrinks more and more closely round the corpuscles, and a fairly solid, trembling, jelly-like clot, which can be cut with a knife, is formed. During this time the clot takes the shape of the vessel in which the blood coagulates, and expresses from its substance a fluid—the **blood-serum**. Fibrin may be obtained by washing away the corpuscles from the clot with a stream of water.

Crusta Phlogistica.—If the corpuscles subside very rapidly, and if the blood coagulates slowly, the upper stratum of the clot is not red, but only yellowish, on account of the absence of coloured corpuscles. This is regularly the case in horse's blood, and in human blood it is observed especially in inflammations; hence this layer has been called **crusta phlogistica**. Such blood contains more fibrin, and so coagulates more slowly.

The crusta is formed under other circumstances, *e.g.*, with increased sp. gr. of the corpuscles, or diminished sp. gr. of the plasma (as in hydremia and chlorosis), whereby the corpuscles sink more rapidly, and also during pregnancy. The taller and narrower the glass, the thicker is the crusta (compare § 41). The upper end of the clot, where there are few corpuscles, shrinks more, and is therefore smaller than the rest of the clot. This upper, lighter-coloured layer is called the "**buffy coat**"; but it gradually passes both in size and colour into the normal dark-coloured clot. [Sometimes the upper surface of the clot is concave or "**cupped**." The older physicians attached great importance to this condition, and also to the occurrence of the buffy coat.]

Defibrinated Blood.—If freshly-shed blood be beaten or whipped with a glass rod, or with a bundle of twigs, fibrin is deposited on the rod or twigs in the form of a solid, fibrous, yellowish-white, elastic mass, and the blood which remains is called "**defibrinated blood**" (p. 34). [The twigs and fibrin must be washed in a stream of water to remove adhering corpuscles.]

Coagulation of Plasma.—Plasma shows phenomena exactly analogous, save that the clot is not so well marked, owing to the absence of the resisting corpuscles; there is, however, always a soft trembling jelly formed when plasma coagulates. [In Hewson's experiment on the blood of a horse tied in a vein, he found that the plasma coagulated—fibrin being formed, so that he showed coagulation to be due to changes in the plasma itself (§ 29).]

Properties of Fibrin.—Although the fibrin appears voluminous, it only occurs to the extent of 0·2 per cent. (0·1 to 0·3 per cent.) in the blood. The amount varies considerably in two samples of the same blood. It is insoluble in water and ether; alcohol shrivels it by extracting water; dilute hydrochloric acid (0·1 per cent.) causes it to swell up and become clear, and changes it into syntonin or acid-albumin (§ 249, III.). When fresh, it has a greyish-yellow fibrous appearance, and is elastic; when dried, it is horny, transparent, brittle, and friable.

When fresh it dissolves in 6-8 per cent. solution of sodium nitrate or sulphate, in dilute alkalis, and in ammonia, thus forming alkali-albuminate. Heat does not coagulate these

solutions. [It is also soluble in, or rather decomposed by, 5–10 per cent. solutions of neutral salts, *e.g.*, NaCl, yielding two fibro-globulins (*Green*).] Hydric peroxide is rapidly decomposed by fibrin into water and O (*Thénard*). Fibrin which has been exposed to the air for a long time is no longer soluble in solution of potassic nitrate, but in neurin (*Mauthner*). During putrefaction it passes into solution, albumin being formed. Fibrin contains, entangled in it, ferrie, calcic, and magnesian phosphates, and calcium sulphate, whose origin is unknown. [The ash of fibrin contains .88 to .95 per cent. of calcic phosphate.]

Time for Coagulation.—The first appearance of a coagulum occurs in man's blood after 3 minutes 45 seconds, in woman's blood after 2 min. 20 sec. (*H. Nasse*). Age has no effect; withdrawal of food accelerates coagulation (*H. Vierordt*).

28. GENERAL PHENOMENA OF COAGULATION.—I. Blood in direct contact with living unaltered blood-vessels does not coagulate. [Hewson (1772) found that when he tied the jugular vein of a horse in two places, and excised it, the blood did not coagulate for a long time.] Brücke filled the heart of a tortoise with blood which had stood 15 minutes exposed to the air at 0°, and kept it in a moist chamber; at 0° C. the blood was still uncoagulated in the contracting heart after eight days. Blood in a contracting frog's heart preserved under mercury does not coagulate. If the wall of the blood-vessel be altered by **pathological processes** (*e.g.*, if the intima becomes rough and uneven, or undergoes inflammatory change), coagulation is apt to occur at these places. Blood rapidly coagulates in a *dead* heart, or in blood-vessels (but not in capillaries) or other canals (*e.g.*, the ureter). If blood stagnates in a living vessel, coagulation begins in the central axis, because here there is no contact with the wall of the living blood-vessel.

II. **Conditions which Hinder or Delay Coagulation.**—(a) The addition of small quantities of *alkalies*, *ammonia*, or concentrated solutions of *neutral salts of the alkalies and earths* (alkaline chlorides, sulphates, phosphates, nitrates, carbonates). Magnesian sulphate acts most favourably in delaying coagulation (1 vol. solution of 28 per cent. to 3½ vols. blood of the horse).

(b) Precipitation of the fibrino-plastin by adding weak acids, or CO₂.

By the addition of *acetic acid* until the reaction is acid, coagulation is completely arrested. A large amount of CO₂ delays it, hence venous blood coagulates more slowly than arterial, and the blood of *suffocated* persons remains fluid for the same reason.

(c) The addition of *egg-albumin*, *syrup*, *glycerine*, and much *water*. If uncoagulated blood be brought into contact with a layer of already-formed fibrin, coagulation occurs later.

(d) By *cold* (0° C.) coagulation may be delayed for one hour. If blood is frozen at once, after thawing it is still fluid, and then coagulates (*Hewson*). When shed blood is under *high pressure* it coagulates slowly.

(e) Blood of *embryo-fowls* does not coagulate before the twelfth or fourteenth day of incubation (*Boll*); that of the *hepatic vein* very slightly; *menstrual blood* shows little tendency to coagulate when alkaline mucus from the vagina is mixed with it. If it be rapidly discharged, it coagulates in masses. Foetal blood at the moment of birth coagulates soon.

(f) *Blood rich in fibrin* from inflamed parts coagulates slowly, but the clot so formed is firm.

(g) [Blood coagulates more slowly in a smooth than a rough vessel, and also in a shallow vessel than in a deep one.]

(h) Blood in contact with pure oil coagulates more slowly than when it is in contact with glass or metal. Even a tube or vessel smeared with oil or vaseline delays coagulation, so that blood flows longer through such a tube without coagulating than through a glass or metal tube. The action seems to be a purely physical one between the blood and the oil.]

(i) Absence of oxygen.

Injection of Peptones (albumoses) and other bodies.—Albertoni observed that if tryptic pancreas ferment (dissolved in glycerine) be injected into the blood of an animal, the blood

when shed does not coagulate. Schmidt-Mülheim found that after the injection of *peptone* into the blood (0·5 gram per kilo.) of a dog, the blood lost its power of coagulating. [This occurs in the dog, but not in the rabbit. Peptonised blood coagulates when it is treated with CO_2 or water. It appears, however, that it is not the peptone which prevents the coagulation, but the *albumoses* adhering to it which do so.] A substance is formed in the plasma, which prevents coagulation, but which is precipitated by CO_2 . Lymph behaves similarly (*Fano*). After peptones are injected, there is a great solution of leucocytes in the blood (*v. Samson-Himmelstjerna*). The secretion of the mouth of the medicinal leech, [although its action is not due to a ferment (*Haycraft*)], and snake poison also prevent coagulation (*Wall*). [Diastatic ferment (*Salvioli*) and the poisonous substance in the serum of eels' blood (*Mosso*) also prevent coagulation.]

Hæmophilia.—A very slight scratch in some persons may cause very free bleeding. These persons are called colloquially “bleeders,” and are said to have *hæmophilia* or the *hæmorrhagic diathesis*. In “bleeders” coagulation seems not to take place, owing to a want of the substances producing fibrin; hence, in these cases, wounds of vessels are not plugged with fibrin. [A tendency to hæmorrhage occurs in scurvy, purpura, in some infectious diseases, such as typhus, plague, yellow fever, and in poisoning with phosphorus.]

[Leech Extract.]—A watery extract of the buccal cavity of the leech—the secretion probably is derived from the epithelial cells lining the sucker and buccal cavity—when injected into the blood-vessels of a dog or rabbit, or mixed with the uncoagulated blood of these animals, prevents coagulation for a much longer time than is the case with the injection of so-called peptones, for it is really the albumoses mixed with the peptones which prevent coagulation in the blood of the dog. The action of leech-extract, like that of the products of digestion, is not permanent. When injected it produces far milder constitutional symptoms than albumose, but its action on the blood is far more powerful. It is eliminated by the kidneys. So far this active principle has not been isolated, although it is soluble in water, saline solutions, and insoluble in alcohol, ether, and chloroform (*Haycraft*).]

III. Coagulation is accelerated—(a) By contact with foreign Substances of all kinds, but only when the blood adheres to them, hence threads or needles introduced into arteries are rapidly covered with fibrin. [The coagulation always begins around the foreign body.] Blood does not coagulate in contact with bodies covered with fat or vaseline (*Freund*). Even the introduction of air-bubbles into the circulation or the passage of indifferent gases, N or H, through blood, accelerates it. The pathologically altered wall of a vessel acts like a foreign body. Blood shed from an artery rapidly coagulates on the walls of vessels, on the surfaces exposed freely to air, and on the rods or twigs used to beat it.

(b) The products of the retrogressive metabolism of proteids (uric acid, glycin, leucin, taurin, kreatin, sarkin, but not urea) favour coagulation by increased ferment-formation; but if they are added in excess, they retard the process.

(c) From a watery extract of the testis or thymus, on the addition of acetic acid, is precipitated a substance which is soluble in sodic carbonate. It is a mixture of *lecithin* and albumin, and when it is injected into the blood-stream it causes almost instantaneous death by intravascular coagulation (*Woodbridge*). [Injection of a watery extract of the thymus, supra-renal capsules, and testis suffice to produce extensive intra-vascular clotting, and even the injection of laky blood accelerates coagulation.]

(d) During rapid hæmorrhage, the last portions of blood coagulate most rapidly (*Holzmann*).

(e) Heating the blood from 39° to 55° C. (*Hewson*).

(f) Agitation of the blood (*Hewson and Hunter*).

[(g) The addition of a small quantity of water.

(h) A *watery* condition of the blood. The clot is small and soft.

(i) Contact with oxygen, or free exposure to the air.

But contact with oxygen is not necessary for coagulation to take place, as this occurs in contact with indifferent gases, as well as in a vacuum.]

IV. Rapidity of Coagulation.—Amongst vertebrates, the blood of birds (especially of the pigeon) coagulates almost momentarily; in cold-blooded animals coagulation occurs much more slowly, while mammals stand midway between the two.

[The blood of a fowl begins to coagulate in $\frac{1}{2}$ to $1\frac{1}{2}$ minute; pig, sheep, rabbit, in $\frac{1}{2}$ to $1\frac{1}{2}$ minute; dog, 1 to 3 minutes; horse and ox, 5 to 13 minutes; man, 3 to 4 minutes; solidifica-

tion is completed in 9 to 11 minutes (*Nasse*).] The blood of invertebrates, which is usually colourless when it is oxidised (§ 32), forms a soft, whitish clot of fibrin. Even in lymph and chyle a small soft clot is formed.

V. When coagulation occurs, the aggregate condition of the fibrin-factors is altered, so that **heat** must be **set free** (*Valentin*, 1844).

VI. In blood shed from an artery, the degree of **alkalinity diminishes** from the time of its being shed until coagulation is completed (*Pflüger and Zuntz*). This is probably due to a decomposition in the blood, whereby an acid is developed, which diminishes the alkalinity (p. 2).

VII. During coagulation there is a **diminution of the O** in the blood, although a similar decrease also occurs in non-coagulated blood. Traces of *ammonia* are also given off, which Richardson erroneously supposed to be the cause of the coagulation of the blood.

[This is refuted—(1) by the fact that blood, when collected under mercury (whereby no escape of ammonia is possible) also coagulates; and (2) by the following experiment of Lister:—He placed two ligatures on a vein containing blood, moistening one-half of the outer surface of the vein with ammonia, leaving the other half intact. The blood coagulated in the first half, and not in the other, owing to the properties of the wall of the vein of the former being altered. Neither the decrease of O nor the evolution of ammonia seems to have any causal connection with the formation of fibrin.]

Pathological.—When the blood coagulates within the vessels during life, the process is called **thrombosis**, and the coagulum or plug so formed is termed a **thrombus**. When a clot of blood or other body is carried by the blood-stream to another part of the vascular system where it blocks up a vessel, the plug is called an **embolus**, and the result **embolism**.

Coagulable Fluids.—With regard to coagulability, fluids containing proteids may be classified thus:—

- (1) Those that *coagulate spontaneously*, *i.e.*, blood, lymph, chyle.
- (2) Those *capable of coagulating*, *e.g.*, fluids secreted pathologically in serous cavities; for example, hydrocele fluid, which, as usually containing fibrinogen only, does not coagulate spontaneously, but it coagulates on the addition of fibrino-plastin and ferment (or of blood-serum, in which both occur).
- (3) Those which *do not coagulate*, *e.g.*, milk or seminal fluid, which do not seem to contain fibrinogen.

29. CAUSE OF THE COAGULATION OF BLOOD.—[*Hewson's Experiments* (1772).—Hewson tied the jugular vein of a horse between two ligatures, removed it, and then suspended it by one end (fig. 28). He found that the blood remained fluid for a long time (48 hours), the red corpuscles sank (RC), and left a clear layer of plasma on the surface (P). On drawing off some of this clear plasma it coagulated, thus proving coagulation to be due to changes in the plasma. If a glass rod be pushed through the wall of the vessel into the fluid, coagulation begins around the foreign body. The glass rod, however, must not be perfectly smooth. Lister repeated this experiment, and found that, even if the upper end of the tube be opened and the blood freely exposed to the air, coagulation is but slightly hastened. He showed that the blood might be poured from one vein into another, just as one might pour fluid from one test-tube into another. In this case there were two test-tubes, *i.e.*, the veins—and although the blood, on being poured from the one to the other, came into contact with the air, it did not coagulate. Hewson, however, found that blood poured from the vein into a glass vessel coagulated, so that, in his opinion, the blood-vessels exerted a restraining influence on coagulation. By cooling the blood and preventing it from coagulating, he proved that coagulation was not due to the loss of heat. Nor could it be a vital act, as sodie sulphate or other neutral salt prevented coagulation indefinitely, but coagulation took place when the blood was diluted with water.]

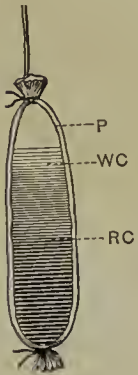


Fig. 28.

Vein of horse tied between two ligatures. P, plasma; WC, white, and RC, red corpuscles.

[**Buchanan's Researches.**—The serous sacs of the body contain a fluid which in some respects closely resembles lymph. The pericardial fluid of some animals coagulates spontaneously (*e.g.*, in the rabbit, ox, horse, and sheep) if the fluid be removed *immediately after death*. If this be not done till *several hours after death*, the fluid does not coagulate spontaneously. The fluid of the tunica vaginalis of the testis sometimes accumulates to a great extent, and constitutes *hydrocele*, but this fluid shows no tendency to coagulate spontaneously. Andrew Buchanan found, however, that if to the fluid of ascites, pleuritic fluid, or hydrocele fluid, there be added clear blood-serum, then coagulation takes place, *i.e.* two fluids—neither of which shows any

tendency *by itself* to coagulate—form a clot when they are mixed (1831). He also found that if “washed blood-clot” (which consists of a mixture of fibrin and colourless corpuscles) be added to hydrocele fluid, coagulation occurred. He compared the action of washed blood-clot to the action of rennet in coagulating milk, and he imagined *the agents which determined the coagulation to be colourless corpuscles*. Thus, the buffy coat of horses’ blood is a powerful agent, and it contains numerous colourless corpuscles. He finally concluded that some constituent in the plasma, to which he gave the name of a “soluble fibrin,” is acted upon by the colourless corpuscles and converted into fibrin. The soluble fibrin of Buchanan is comparable to the fibrinogen in Hammarsten’s theory. Buchanan, however, did not separate the substance.]

[**Denis’s Plasmine** (1859).—Denis mixed uncoagulated blood with a saturated solution of sodic sulphate, and allowed the corpuscles to subside. The salted plasma thus obtained he precipitated with sodic chloride. The precipitate, when washed with a saturated solution of sodic chloride, he called **plasmine**. If plasmine be mixed with water, it coagulates spontaneously, resulting in the formation of fibrin, while another proteid remains in solution. According to the view of Denis, fibrin is produced by the splitting up of plasmine into two bodies—fibrin and a soluble proteid.]

[If to plasma, *e.g.*, from horse’s blood, there be added NaCl to the extent of 13 per cent., a white viscid precipitate is thrown down. If this precipitate be removed, and more NaCl added, or MgSO_4 crystals, another proteid, white and granular, is precipitated. The former is **fibrinogen**, and the latter **para-globulin**, so that the so-called plasmine of Denis really consists of two proteids; only the former, however, is converted into fibrin.]

[**Brücke’s experiments** were directed to the question why the blood does not coagulate within the vessels. Hewson had shown that blood remains fluid for 6–14 hours in the vessels after the death of the animal (dog). In the case of cold-blooded animals, *e.g.*, the turtle at $+1^\circ \text{C}$, the blood remained fluid for six to eight days. Again, the blood remained fluid in the excised heart of a turtle kept moist under a bell jar as long as the heart continued to beat and until the cardiac walls lost their excitability. A foreign body introduced into the blood-vessels was soon surrounded with a clot of fibrin, which was always deposited on the foreign body itself and not on the walls of the blood-vessels. The same results were obtained in mammals, and especially in new-born animals. This action of the vascular wall in preventing coagulation only exists as long as the wall itself is intact and alive.]

[**Lister** maintained that the blood has no spontaneous tendency to clot, as Brücke supposed, but that it only clots when brought into contact with foreign matter, and this is the view now generally held.]

[**A. Schmidt’s Researches** (1861).—This observer rediscovered the chief facts already known to Buchanan, *viz.*, that some fluids which do not coagulate spontaneously clot when mixed with other fluids, which show no tendency to coagulate spontaneously, *e.g.*, hydrocele fluid and blood-serum. He isolated from these fluids the bodies described as fibrinogen and fibrino-plastin. The bodies so obtained were not pure, but Schmidt supposed that the formation of fibrin was due to the interaction of these two proteids. The reason hydrocele fluid does not coagulate, he says, is that it contains fibrinogen and no fibrino-plastin, while blood-serum contains the latter, but not the former. Schmidt afterwards discovered that these two substances may be present in a fluid, and yet coagulation may not occur (*e.g.*, occasionally in hydrocele fluid). He supposed, therefore, that blood or blood-serum contained some other constituent necessary for coagulation. This he afterwards isolated in an impure condition and called *fibrin-ferment*.]

A. Schmidt’s theory of Coagulation is that fibrin is formed by the coming together of *two proteid substances* which occur dissolved in the plasma, *viz.*:—(1) **fibrinogen**, *i.e.*, the substance which yields the chief mass of the fibrin, and (2) **fibrino-plastic substance** or fibrino-plastin. The latter terms are now rarely used, having been replaced by either of the following—serum-globulin or para-globulin, § 32. In order to determine the coagulation a ferment seems to be necessary, and this is supplied by (3) the **fibrin-ferment**. [Reviewing all the evidence, it seems quite certain that para-globulin is not concerned in the process of coagulation, so that Schmidt’s theory has now given place to that of Hammarsten (p 41).]

1. Properties of Fibrinogen and fibrino-plastin.—They belong to the group of proteids called **globulins**, *i.e.*, they are insoluble in pure water, but are soluble in dilute saline solutions (*e.g.*, common salt, § 249), and are not distinguished from each other by well-marked chemical characters. Still they differ as follows:—

Fibrino-plastin or **Serum-globulin** is more easily precipitated from its solutions than fibrinogen. It is more readily redissolved when once it is precipitated. It forms when precipitated a very light granular powder, [and its saline solution coagulates at 75°C .]

Fibrinogen adheres as a sticky deposit to the side of the vessel. It coagulates at 56°C .

On account of their great similarity, both substances are not usually prepared from blood-plasma. *Fibrinogen* is prepared from *serous* transudations (pericardial, abdominal, or pleuritic fluid, or the fluid of hydrocele), which contain no fibrinoplastin. *Fibrinoplastin* is most readily prepared from *serum*, in which there is still plenty of fibrinoplastin, but no fibrinogen.

2. **Preparation of Fibrinoplastin, Serum-globulin, or Paraglobulin.**—(a) Dilute **blood-serum** with twelve times its volume of ice-cold water, and almost neutralise it with acetic acid [add 4 drops of a 25 per cent. solution of acetic acid to every 120 c.c. of diluted serum]; or (b) pass a stream of carbon dioxide through the diluted serum, which soon becomes turbid; after a time a fine white powder, copious and granular, is precipitated.

[(c) **Method of Hammarsten for Serum-globulin.**—All the serum-globulin in serum is not precipitated either by adding acetic acid or by CO_2 . Hammarsten found, however, that if crystals of magnesium sulphate be added to complete saturation, it precipitates the serum-globulin, but does not precipitate serum-albumin; serum-globulin is more abundant than serum-albumin in the serum of the ox and horse, while in man and the rabbit the reverse obtains; (compare § 32).]

Schmidt found that 100 c.c. of the serum of ox blood yielded 0.7 to 0.8 grm.; horse's serum, 0.3 to 0.56 grm. of dry fibrinoplastin. Fibrinoplastin occurs not only in serum, but also in red blood-corpuscles, in the fluids of connective-tissue, and in the juices of the cornea.

3. **Preparation of Fibrinogen.**—This is best prepared from **hydrocele fluid**, although it may also be obtained from the fluids of serous cavities, *e.g.*, the pleura, pericardium, or peritoneum. It does not exist in blood-serum, although it does exist in blood-plasma, lymph, and chyle, from which it may be obtained by a stream of CO_2 , after the paraglobulin is precipitated. (a) Dilute hydrocele fluid with ten to fifteen times its volume of water, and pass a stream of CO_2 through it for a long time. (b) Add powdered *common salt* to saturation to a serous transudation, when a sticky glutinous (not very abundant) precipitate of fibrinogen is obtained.

[Hammarsten and Eichwald find that, although paraglobulin and fibrinogen are soluble in solutions of common salt (containing 5 to 8 per cent. of the salt), a saline solution of 12 to 16 per cent. is required to precipitate the fibrinogen, leaving still in solution paraglobulin, which is not precipitated until the amount of salt exceeds 20 per cent.]

Properties of the so-called Fibrin-Factors.—They are insoluble in pure water, but dissolve in water containing O in solution. Both are soluble in very dilute alkalis, *e.g.*, caustic soda, and are precipitated from this solution by CO_2 . They are soluble in dilute saline solutions, *e.g.*, of common salt—like all globulins—but if a certain amount of common salt and some other salts, *e.g.*, MgSO_4 , be added in excess, they are precipitated. Very dilute hydrochloric acid dissolves them, but after several hours they become changed into a body resembling syntonin or acid-albumin (§ 249, III.). Fibrinogen held in solution by common salt coagulates at 52° to 55°C . [Fredericq finds the fibrinogen exists *as such* in the plasma; it coagulates at 56°C ., and the plasma thereafter is uncoagulable spontaneously.]

4. **Preparation of the Fibrin-Ferment.**—(a) Mix blood-serum (ox) with twenty times its volume of strong alcohol, and after one month filter off the deposit thereby produced. The deposit on the filter consists of coagulated insoluble albumin and the ferment; dry it carefully over sulphuric acid, and reduce to a powder. Triturate 1 gram of the powder with 65 c.c. of water for ten minutes, and filter. The ferment is dissolved by the water, and passes through the filter, while the coagulated albumin remains behind.

[(b) **Gamgee's Method.**—Buchanan's "washed blood-clot" (p. 39) is digested in an 8 per cent. solution of common salt. The solution so obtained possesses in an intense degree the properties of Schmidt's fibrin-ferment.]

In the preparation of fibrino-plastin, the ferment is carried down with it mechanically. The ferment seems to be formed first in fluids outside the body, very probably by the dissolution of the colourless corpuscles. More ferment is formed in the blood the longer the interval between its being shed and its coagulation. It is destroyed at 70° C. Blood flowing directly from an artery into alcohol contains no ferment. It is also formed in other protoplasmic parts (*Rauschenbach*), e.g., in dead muscle, brain, supra-renal capsule, spermatozoa, testicle (*Foa and Pellacani*), and in vegetable micro-organisms [e.g., yeast] and protozoa (*Grohmann*), [so that it would seem to be a general product of protoplasm. As the ferment does not pre-exist in colourless blood-corpuscles, it seems to be formed from some mother-substance in them, the blood-plasma itself decomposing this substance.]

Coagulation Experiments.—According to A. Schmidt, if pure solutions of (1) fibrinogen, (2) fibrino-plastin, and (3) fibrin-ferment be mixed, fibrin is formed. [As we have already seen, (2) is not essential.] The process goes on best at the temperature of the body; it is delayed at 0°; and the ferment is destroyed at the boiling-point. The presence of O seems necessary for coagulation. The amount of the ferment appears to be immaterial; large quantities produce more rapid coagulation, but the amount of fibrin formed is not greater.

[*Foa and Pellacani* find that a filtered watery extract of fresh brain, supra-renal capsules, testis, thymus, and some other tissues, when injected into the blood-vessels of a rabbit, causes coagulation of the blood in the pulmonary circulation and the heart, death being caused by the action of a substance identical with the fibrin-ferment.]

[Nature of the fibrin-ferment.]—It is a proteid belonging to the group of the globulins, and, according to Halliburton, it has the properties of a cell-globulin, i.e., a globulin obtained from the disintegration of cells, e.g., leucocytes or lymph-corpuscles (p. 33). The fibrin-ferment is (almost) identical with this cell-globulin. A very considerable quantity of active blood-ferment may be injected into the blood-vessels of a living animal without causing coagulation within the blood-vessels. It may be that the ferment is destroyed within the vascular system.]

[What the exact nature of the action of fibrin-ferment is on the fibrinogen in shed blood we do not know; but the amount of fibrin formed is always slightly less than the amount of fibrinogen acted on, there being always formed a small amount of another globulin. If the solution of fibrin-ferment be boiled, all its coagulation-determining properties are at once and permanently destroyed.]

The **amount of salts** present has a remarkable relation to coagulation. Unless a certain amount of salts be present in the fluid (1 per cent. NaCl), coagulation takes place slowly or partially. Freund has shown that the process of coagulation is always accompanied by an excretion of phosphates of the alkaline earths. Fibrin contains a constant amount of phosphates of the alkaline earths (p. 36). Coagulable fluids coagulate after the addition of these salts; they do not coagulate in the absence of these salts. The action of adhesion (p. 37) in accelerating coagulation is said to depend on the occurrence of the interaction during life of the phosphoric acid or alkaline phosphates present specially in the cellular elements of the blood with the lime and magnesia salts present especially in the plasma. [Green finds that calcium sulphate brings about coagulation in plasma which shows little or no tendency to clot, while coagulation in its absence is almost or quite prevented.]

[Ringer and Sainsbury have studied the influence of salts on the clotting of blood (and also certain pathological fluids, e.g., of ascites, hydrocele fluid, and milk). They confirm Green's statement that calcium sulphate is an essential to the act of clotting, but they find that calcium chloride also acts very efficiently in determining coagulation. The salts of strontium and barium act like those of calcium sulphate, but are less powerful. The soda and potash salts (NaCl and KCl), on the other hand, restrain, prolong, or prevent the act of coagulation; but the soda salts are rather more powerful than the potassium salts. The addition of lime salts overcomes the restraining influence of the soda and potash salts, so that there is an antagonism between the salts of lime on the one hand, and of potassium and sodium on the other.]

When blood or blood-plasma coagulates, all the fibrinogen is used up, so that the serum contains only fibrino-plastin and fibrin-ferment; hence the addition of hydrocele fluid (which contains fibrinogen) to serum causes coagulation.

[Hammarsten's Theory of Coagulation.]—Hammarsten's researches led him to believe that fibrino-plastin is quite unnecessary for coagulation. According to him, fibrin is formed from *one* body, viz., **fibrinogen**, which is present in plasma when it is acted upon by the **fibrin-ferment**; the latter, however, has not been obtained in a pure state. Neither he nor Schmidt assert that this body is of the

nature of a ferment, although they use the term for convenience. It is quite certain that fibrin may be formed when no fibrino-plastin is present, coagulation being caused by the addition of calcic chloride or casein prepared in a special way. One of the conditions necessary for the action of fibrin-ferment on fibrinogen seems to be the presence of neutral salts. If the latter be completely removed the formation of fibrin does not take place. Lime salts seem to be in some way essential to the process, *e.g.*, calcic sulphate, while others attach importance to the presence of NaCl.]

[The main drift of the foregoing evidence points to the presence of one proteid—**fibrinogen**—which exists dissolved in the blood-plasma, and which under certain circumstances yields fibrin. In shed blood this act seems to be determined by a ferment, perhaps derived from the disintegration of colourless corpuscles (and blood-platelets?), which occurs when blood is shed.]

[It must not be forgotten that the presence of certain **salts** seems necessary to the act of coagulation. As the question at present stands, three factors are recognised in the equation :—

- (1) A coagulable proteid (fibrinogen).
- (2) A ferment.
- (3) Certain salts.

Up till recently the first two have attracted the greatest amount of attention, but that the third factor is also an important one is shown by the above-mentioned researches.]

30. SOURCE OF THE FIBRIN-FACTORS—Al. Schmidt maintains that all the three substances out of which fibrin, according to him, is formed arise from the breaking up of colourless blood-corpuscles. In the blood of man and mammals fibrinogen exists dissolved in the circulating blood as a dissolution-product of the retrogressive changes of the white corpuscles. Plasma contains dissolved fibrinogen and serum-albumin. The circulating blood is very rich in colourless blood-corpuscles—much richer, indeed, than was formerly supposed. As soon as blood is shed from an artery, enormous numbers of the colourless corpuscles are dissolved—according to Al. Schmidt, 71·7 per cent. (horse). First the body of the cell disappears, and then the nucleus. The products of their dissolution are dissolved in the plasma, and one of these products is *fibrino-plastin*. At the same time the fibrin-ferment is also produced, so that it would seem not to exist in the intact blood-corpuscles. Fibrino-plastin and fibrin-ferment are also produced by the “*transition forms*” of blood-corpuscles, *i.e.*, those forms which are intermediate between the red and the white corpuscles. They seem to break up immediately after blood is shed. The *blood-plates* (p. 19) are also, probably, sources of these substances.

The leucocytes have different degrees of resistance; those of the lymph and chyle are more resistant than those of the blood, and amongst the latter themselves there are various degrees (*Heyl*).

In amphibians and birds the *red* nucleated corpuscles rapidly break up after blood is shed, and yield the substance or substances which form fibrin. Al. Schmidt convinced himself that in these animals fibrinogen is originally a constituent of the blood-corpuscles.

It is clear, therefore, according to Schmidt's view, that as soon as the blood-corpuscles, white or red, are dissolved, the fibrin-factors pass into solution, and the formation of fibrin by the interaction of the three substances will ensue.

If a large number of leucocytes be introduced into the circulation of an animal, the leucocytes are dissolved in great numbers in the blood, so that death takes place by diffuse coagulation. Should the animal survive the immediate danger of death, the blood, owing to the want of leucocytes, is completely incapable of coagulating (*Groth*).

[And. Buchanan thought that the potential element of his “washed blood-clot” resided in the colourless corpuscles, “primary cells or vesicles.” He, like Schmidt, found that the buffy coat of horses' blood, which is very rich in white corpuscles, produced coagulation rapidly. Buchanan compared the action of his washed clot to that of rennet in coagulating milk.]

Pathological.—Al. Schmidt and his pupils have shown that *some* ferment, probably derived from the dissolution of colourless corpuscles, is found in circulating blood, and that it is more abundant in venous than in arterial blood, while it is most abundant in shed blood. It is specially remarkable that in *septic fever* the amount of ferment in blood may increase to such an extent as to permit the occurrence of spontaneous coagulation (thrombosis), which may even produce death (*Arn. Köhler*). In febrile cases generally, the amount of ferment is somewhat more abundant (*Edelberg and Birk*). After the injection of ichor into the blood an enormous

number of colourless corpuscles are dissolved (*F. Hoffmann*). The injection of peptone, Hb, and to a less degree of distilled water, is followed by dissolution of numerous leucocytes.

There are changes in the blood, constituting true blood diseases, in which the physiological metabolism of the colourless corpuscles is enormously increased, so that the metabolic products accumulate in the blood (*Alex. Schmidt*). The result of this is spontaneous coagulation within the circulatory system, and death even may occur; there is always an increase of temperature. After such a condition the coagulability of the blood is diminished.

31. Formation of Fibrin.—After several observers had shown that the red blood-corpuscles (bird, horse, frog) participate in the production of fibrin, Landois observed, in 1874, under the microscope that the stromata of the red blood-corpuscles of mammals passed into fibrin. If a drop of defibrinated rabbit's blood be placed in serum of frog's blood, without mixing them, the red corpuscles can be seen collecting together; their surfaces are sticky, and they can only be separated by a moderate pressure on the cover-glass, whereby some of the now spherical corpuscles are drawn out into threads. The corpuscles soon become spherical, and those at the margin allow the hæmoglobin to escape; the decolorisation progresses, from the margin inwards, until at last there remain masses of stroma adhering together. The stroma-substance is very sticky, but soon the cell-contours disappear, and the stromata adhere and form fine fibres. Thus (according to Landois) the formation of fibrin from red blood-corpuscles can be traced step by step. The red corpuscles of man and animals, when dissolved in the serum of other animals, show much the same phenomena.

Stroma-Fibrin and Plasma-Fibrin.—Landois calls fibrin formed direct from stroma, *stroma-fibrin*; fibrin formed in the usual way, *plasma-fibrin*. The stroma-fibrin is closely related chemically to stroma itself; as yet, however, the two kinds of fibrin have not been sharply distinguished chemically. Substances which rapidly dissolve red corpuscles cause extensive coagulation, e.g., injection of bile or bile salts, or lake-coloured blood, into arteries. After the injection of foreign blood the newly-injected blood often breaks up in the blood-vessels of the recipient, while the finer vessels are frequently found plugged with small thrombi (§ 102).

32. CHEMICAL COMPOSITION OF PLASMA AND SERUM.—I. **Proteids** occur to the amount of 8 to 10 per cent. in the plasma. Only 0·2 per cent. of these go to form fibrin. After the formation of the fibrin the plasma is converted into serum. The sp. gr. of human serum is 1027 to 1029. It contains several proteids. [According to Hammarsten, *human* serum contains 9·207 per cent. of solids,—of these, 3·103 = serum-globulin, and 4·516 = serum-albumin, i.e., in the ratio of 1 : 1·511. In horse-serum the proportion is 4·5 : 2·6, in ox-serum 4·16 : 3·329, and rabbit-serum 1·78 : 4·43. The total amount of proteids in blood seems to be much more constant than are the relative proportions of serum-albumin and serum-globulin (*Salvioli*).]

[The following table, compiled by Gamgee from Hammarsten's researches, shows that the proportion of serum-globulin to serum-albumin varies remarkably; in some cases serum-globulin is the most abundant proteid in the serum of some animals, while in others it is the reverse :—

Variety of Serum.	Total solids in 100 parts.	Total proteids in 100 parts.	Serum-globulin in 100 parts.	Serum-albumin in 100 parts.	Lecithin, fat, salts, &c., in 100 parts.	Ratio of Serum-globulin to Serum-albumin.
From blood of horse,	8·597	7·257	4·565	2·677	1·340	1 : 0·591
„ „ ox, .	8·965	7·499	4·169	3·329	1·466	1 : 0·842
„ „ man, .	9·207	7·619	3·103	4·516	1·587	1 : 1·511
„ „ rabbit,	7·525	6·225	1·788	4·436	1·299	1 : 2·5]

(a) **Serum-globulin or Paraglobulin** (2 to 4 per cent.). If crystals of magnesium sulphate be added to saturation to serum at 35° C., serum-globulin is precipitated, but not serum-albumin. It is soluble in 10 per cent. solution of common salt, and coagulates at 69–75° C. Its specific rotatory power is –47°·8 (*Fredericy*).

[Serum-globulin was described by Panum under the name of “serum-casein”; by Al. Schmidt, as “fibrino-plastic substance”; and by Kühne, as “paraglobulin.”]

(b) **Serum-albumin** (3-4 per cent.). Its solution begins to be turbid at 60°C. , and coagulation occurs at 73°C. , the fluid becoming slightly more alkaline at the same time. If sodium chloride be cautiously added to serum, the coagulating temperature may be lowered to 50°C. Its specific rotatory power is from -62.6 to -64.5° (*Starke*). It is changed into syntonin or acid-albumin by the action of dilute HCl , and by dilute alkalis into alkali-albuminate.

[**Effects of Starvation.**—Starvation diminishes the quantity of albumin, and increases the quantity of globulin. During the time a Rhine salmon is in fresh water, it eats nothing; the muscles lose 30 per cent. of their weight, and the testes and ovaries increase at the expense of the muscles (*Miescher*), and at the same time the globulins of the blood—closely related to the globulins of muscle—are increased in amount, the maximum of this increase corresponding to the maximum growth of the ovary (*Bunge*). The globulins are increased at the expense of the albumins.]

Serum-albumin is absent from the blood of starving snakes (the alimentary canal being empty), and reappears after they are fed (*Tiegel*), so that in a digesting snake the blood contains both proteids.

[**Serum-Albumin v. Egg-Albumin.**—Although serum-albumin is closely related to egg-albumin, they differ—(a) as regards their action upon polarised light; (b) the precipitate produced by adding HCl or HNO_3 is readily soluble in 4 c.c. of the reagent in the case of serum-albumin, while the precipitate in egg-albumin is dissolved with very great difficulty; (c) egg-albumin, injected into the veins, is excreted in the urine as a foreign body, while serum-albumin is not; (d) serum-albumin is not coagulated by ether, while egg-albumin is, if the solution is not alkaline (§ 249). Serum-albumin has never been obtained free from salts, even when dialysed for a very long time.]

After all the serum-globulin in serum is precipitated by magnesium sulphate, serum-albumin still remains in solution. If this solution be heated to 40 or 50°C. a copious precipitate of non-coagulated serum-albumin is obtained, which is soluble in water. If the serum-albumin be filtered from the fluid, and if the clear fluid be heated to over 60°C. , *Fredericq* found that it becomes turbid from the precipitation of other proteids; the amount of these other bodies, however, is small.

[**Proteids of the Serum.**—*Halliburton* has shown by the method of “fractional heat-coagulation” (*i.e.*, ascertaining the temperature at which a proteid is coagulated, filtering the fluid and again heating the filtrate to a higher temperature), that from the same fluid perhaps two or more proteids, all with different temperatures of coagulation, may be obtained. Care must be taken to keep the reaction constant. He finds that serum-globulin coagulates at 75°C. , while serum-albumin in reality consists of three proteids, which coagulate at different temperatures: (α) at 73° , (β) at 77° , and (γ) at 84°C.]

[**Precipitation by Salts.**—Sulphate of magnesia not only precipitates serum-globulin, but also fibrinogen. The fluid must be shaken for several hours to get complete saturation. Sodie sulphate, when added to serum deprived of its globulin by MgSO_4 , precipitates serum-albumin, but it produces no precipitate with pure serum. In this way serum-albumin may be obtained in a pure, uncoagulated, and still soluble condition. Serum-globulin is thrown down by sodie nitrate, acetate, or carbonate; while *all* the proteids of the serum are precipitated by potassic acetate or phosphate, and the same result is brought about by adding two salts, *e.g.*, MgSO_4 and Na_2SO_4 (in this case sodio-magnesia sulphate is formed); MgSO_4 and NaNO_3 ; MgSO_4 and KI ; NaCl and Na_2SO_4 . After serum-globulin is thrown down by MgSO_4 , the addition of MgSO_4 and Na_2SO_4 or the double salt, precipitates the serum-albumin, which is still soluble in water. As sulphate of ammonia precipitates all the proteids except peptones, it may be used (*Halliburton*).]

[**The plasma of Invertebrata** (decapod crustaceans, some gasteropods, cephalopods, &c.) clots like vertebrate blood, and contains fibrinogen, but, in addition, there is found in it a substance corresponding to hæmoglobin, and called by *Fredericq*, hæmocyanin. It exists like Hb in two conditions, one reduced and the other oxy-hæmocyanin, the former being colourless, the latter blue. In its general characters it resembles Hb, although it contains *copper* instead of iron, and gives no absorption-bands (*Halliburton*). In the blood of some decapod crustaceans there is a reddish pigment, *tetronerythrin*, which is identical with that in the exoskeleton and hypoderm. It belongs to the group of lipochromes, like some of the pigments of the retina. The hæmocyanin is respiratory in function, and it is remarkable that it is contained in the plasma, and not in the formed elements like the Hb of vertebrates. So that, stated broadly, in these invertebrates the plasma is both nutritive and respiratory in its functions, while in vertebrates the red corpuscles chiefly are respiratory and the plasma nutritive.]

II. **Fats** (0.1 to 0.2 per cent.).—**Neutral fats** (tristearin, tripalmitin, triolein) occur in the blood in the form of small microscopic granules, which, after a meal rich in fat (or milk), render the serum quite milky.

[The amount of fat in the serum of fasting animals is about 0.2 per cent.; during digestion 0.4 to 0.6 per cent.; and in dogs fed on a diet rich in fat it may be 1.25 per cent. There are also minute traces of *fatty acids* (succinic). Röhrig showed that *soluble soaps*, i.e., alkaline salts of the fatty acids, cannot exist in the blood. **Cholesterin** may be considered along with the fats. It occurs in considerable amount in nerve-tissues, and, like fats, is extracted by ether from the dry residue of blood-serum. Hoppe-Seyler found 0.019 to 0.314 per cent. in the serum of the blood of fattened geese. There is no fat in the red blood-corpuscles. **Lecithin** (its decomposition-products, glycerin-phosphoric acid and protagon) occur in serum and also in the blood-corpuscles.]

III. **Traces of Grape-Sugar** [0.1 to 0.15 per cent. (more in the hepatic vein, 0.23 per cent.)] derived from the liver and muscles, and increased after hæmorrhage (§ 175); some **glycogen**, and another reducing fermentative substance.

The amount of **grape-sugar** in the blood increases with the absorption of sugar from the intestine, and this increase is most obvious in the blood of the portal and hepatic veins; there is also a slight increase in the arterial blood, but there it is rapidly exchanged. The presence of sugar is ascertained by coagulating blood by boiling it with sodium sulphate, pressing out the fluid, and testing it for sugar with Fehling's solution (*Cl. Bernard*). Pavy coagulates the blood with alcohol.

IV. **Extractives**.—Kreatin, urea (0.016 per cent., increased after nitrogenous food), succinic acid, and uric acid (more abundant in gouty conditions), guanin (?), carbamic acid, sarcosic acid, all occur in very small amounts.

V. **Salts** (0.85 per cent.), especially *sodic chloride* (0.5 per cent.) and *sodic carbonate*. [It is most important to note that the *soda* salts are far more abundant in the serum than the potassium salts. The ratio may be as high as 10 : 1.] Animal diet increases the amount of salts, vegetable food diminishes it temporarily.

Salts in human blood-serum (*Hoppe-Seyler*).

Sodic Chloride, . . .	4.92 per 1000	Sodic Phosphate, . . .	0.15 per 1000
„ Sulphate, . . .	0.44 „	Calcic Phosphate, . . .	} 0.73 „
„ Carbonate, . . .	0.21 „	Magnesian „, . . .	

If large quantities of salts are introduced into the blood, they almost entirely disappear from the blood-stream within a few minutes, chiefly by diffusion into the tissues. They are gradually eliminated by the kidneys. The same is true of sugar and peptones (*Ludwig and Klicowicz*).

VI. **Water** about 90 per cent.

VII. A yellow pigment.

The pigment may be extracted with methylic alcohol. It shows two absorption-bands of a lipochrome like lutein (*Krukenberg*). Thudichum regards the pigment of the serum as lutein; Maly, as hydrobilirubin; and MacMunn as choletelin.

[**Poisonous Blood-serum**.—The blood-serum of the following genera of fishes—*Anguilla*, *Muraena*, and *Conger*—acts as a powerful poison. Mosso calls the poisonous substance **ichthithoxin**. A dose of 0.02 c.c. per kilogramme weight of a dog is fatal. The action of this body is analogous to that of snake-poison.]

33. **THE GASES OF THE BLOOD**.—**Absorption by Solid Bodies**.—A considerable attraction exists between the particles of solid porous bodies and gases, whereby the latter are attracted and condensed within the pores of solid bodies, i.e., the gases are *absorbed*. Thus, 1 volume of boxwood charcoal (at 12° C. and ordinary barometric pressure) absorbs 35 volumes CO₂, 9.4 vol. O, 7.5 vol. N, 1.75 vol. H. *Heat* is always formed when gases are absorbed, and the amount of heat evolved bears a relation to the energy with which the absorption takes place. Non-porous bodies are similarly invested by a layer of condensed gases on their surface.

By Fluids.—*Fluids* can also absorb gases. A known quantity of fluid at different pressures always absorbs the same volume of gas. Whether the pressure be great or small, the volume of the gas absorbed is equally great (*W. Henry*). But according to Boyle (1662) and Mariotte's law (1679) on the compression of gases, when the pressure within the same volume of gas is increased, the volume varies inversely as the pressure. Hence it follows that, with varying pressure, the volume of gas absorbed remains the same, but the quantity of gas (weight) is

directly proportional to the pressure. If the pressure = 0, the weight of the gas absorbed must also = 0. As a necessary result of this, we see that (1) *fluids can be freed of their absorbed gases in a vacuum under an air-pump.*

Coefficient of Absorption means the *volume* of a gas (0° C.) which is absorbed by a unit of volume of a liquid (at 760 mm. Hg) at a given temperature. The *volume* of a gas absorbed, and therefore the coefficient of absorption, is quite independent of the pressure, while the *weight* of the gas is proportional to it. *Temperature* has an important influence on the coefficient of absorption. With a low temperature it is greatest; it diminishes as the temperature increases; and at the *boiling point* it = 0. Hence it follows that—(2) *absorbed gases may be expelled from fluids simply by causing the fluids to boil.* The coefficient of absorption diminishes for different fluids and gases, with increasing temperature, in a *special*, and by no means uniform, manner, which must be determined empirically for each liquid and gas. Thus the coefficient of absorption for CO_2 in water diminishes with an increasing temperature, while that for H in water remains unchanged between 0° and 20° C.

Diffusion of Gases.—Gases which do not enter into chemical combinations with each other mix with each other in definite proportions. If the necks of two flasks be placed in communication by means of a glass or other tube, and if the lower flask contain CO_2 , and the upper one H, the gases mix *quite independently of their different specific gravities*, both gases forming in each flask a perfectly uniform mixture. The phenomenon is called the *diffusion of gases*. If a *porous membrane* be previously inserted between the gases, the exchange of gases still goes on through the membrane. But (as with endosmosis in fluids) the gases pass with unequal rapidity through the pores, so that at the beginning of the experiment a larger amount of gas is found on one side of the membrane than on the other. According to Graham, the rapidity of the diffusion of the gases through the pores is inversely proportional to the square root of their specific gravities. (According to Bunsen, however, this is not quite correct.)

Different Gases in a Gaseous Mixture do not Exert Pressure upon one another.—Gases, therefore, pass into a space filled with another gas, as they would pass into a vacuum. If the surface of a fluid containing absorbed gases be placed in contact with a very large quantity of another gas, the absorbed gases diffuse into the latter. Hence, absorbed gases can be removed by (3) *passing a stream of another gas through the fluid, or by merely shaking up the fluid with another gas.*

Partial Pressure.—If two or more gases are mixed in a closed space over a fluid, as the different gases existing in a gaseous mixture exert no pressure upon each other, the several gases are absorbed. The weight of each absorbed is proportional to the pressure under which each gas would be, were it the only gas in the space. This pressure is called the *partial pressure* of a gas (*Bunsen*). The absorption of gases from their mixtures, therefore, is *proportional to the partial pressure*. The partial pressure of a gas in a space is at the same time the expression for the tension of the gas absorbed by a fluid.

The air contains 0.2096 volume of O, and 0.7904 volume N. If 1 volume of the air be placed under a pressure, P, over water, the partial pressure under which O is absorbed = $0.2096 P$; that for N = $0.7904 P$. At 0° C., and 760 mm. pressure, 1 volume of water absorbs 0.02477 volume of air, consisting of 0.00862 volume O, and 0.01615 volume N. The absorbed air contains, therefore, 34 per cent. O and 66 per cent. N. *Therefore, water absorbs from the air a mixture of gases containing a larger percentage of O than the air itself.*

34. EXTRACTION OF THE BLOOD GASES.—[The blood to be analysed must be collected over mercury so as to avoid contact with air. This is done by means of a special apparatus, consisting of a graduated tube filled with mercury and communicating with a glass globe also filled with mercury, which can be lowered as the blood flows into the graduated tube.] The extraction of the gases from the blood, and their collection for chemical analysis, are carried out by means of the mercurial pump (*C. Ludwig*). Fig 29 shows in a diagrammatic form the arrangement of Pflüger's gas-pump.

Pflüger's Gas-pump.—It consists of a receptacle for the blood, or "blood bulb" (A), a *glass globe* capable of containing 250 to 300 c.c., connected above and below with tubes, each of which is provided with a stop-cock, *a* and *b*; *b* is an ordinary stop-cock, while *a* has through its long axis a perforation which opens at *x*, and is so arranged that, according to the position of the handle, it leads up into the blood-bulb (position *x*, *a*), or downwards through the lower tube (position *x'*, *a'*). This blood-bulb is first completely emptied of air (by means of a mercurial air-pump), and then carefully weighed. One end (*x'*) of it is tied into an artery or a vein of an animal, and when the lower stop-cock is placed in the position *x*, *a*, blood flows into the receptacle. When the necessary amount of blood is collected, the lower stop-cock is put into the position *x'*, *a'*, and the blood-bulb, after being cleaned most carefully, is weighed to ascertain the weight of the amount of blood collected. The second part of the apparatus consists of the **froth-chamber**, B, leading upwards and downwards into tubes, each of which is provided with an ordinary stop-cock, *c* and *d*. The froth-chamber, as its name denotes, is to catch the froth which is formed during the energetic evolution of the gases from the blood. The lower aperture of the froth-chamber is connected by means of a well-ground tube with the blood-bulb, while above it communicates with the third part of the apparatus, the **drying-chamber**, G. This

consists of a U-shaped tube, provided below with a small glass bulb, which is half filled with sulphuric acid, while in its limbs are placed pieces of pumice-stone, also moistened with sulphuric acid. As the blood gases pass through this apparatus (which may be shut off by the stop-cocks *e* and *f*), they are freed from their *watery vapour* by the sulphuric acid, so that they pass quite dry through the stop-cock, *f*. The short, well-ground tube, *D*, is fixed to *f*, and to the former is attached the small *barometric tube* or *manometer*, *y*, which indicates the extent of the vacuum.

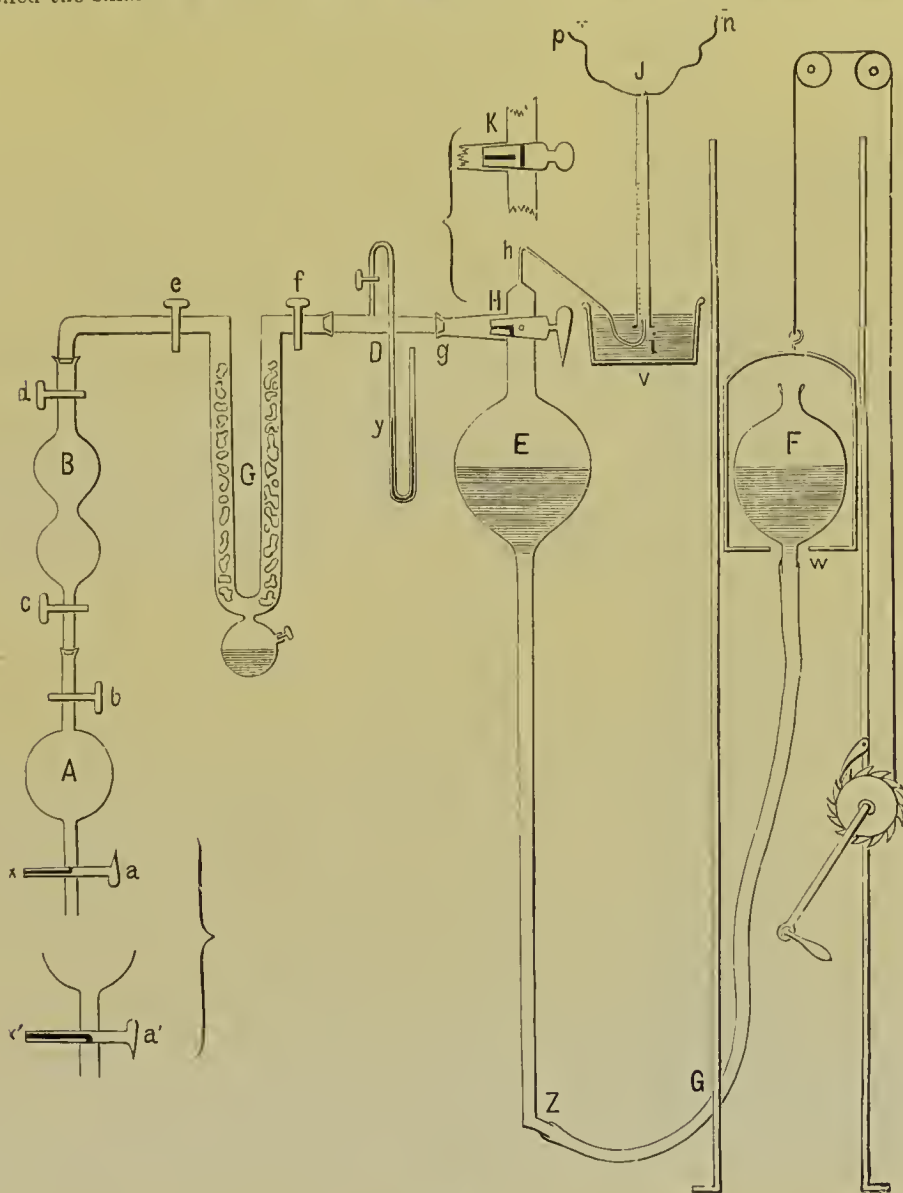


Fig. 29.

Scheme of Pflüger's gas-pump. *A*, blood-bulb; *a*, stop-cock, with a longitudinal perforation, opening upwards; *a'*, the same, opening downwards; *b* and *c*, stop-cocks; *B*, froth-chamber; *d*, *e*, *f*, stop-cocks; *G*, drying-chambers, containing sulphuric acid and pumice-stone; *D*, tube, with manometer, *y*.

From *D* we pass to the **pump** proper. This consists of two large glass bulbs, which are continued above and below into open tubes; the lower tubes, *Z* and *W*, being united by a caoutchouc tube, *G*. Both the bulbs and the caoutchouc tube contain mereury—the bulbs being about half full, and *F* being larger than *E*. The bulb, *E*, is fixed; but *F* can be raised or lowered by means of a pulley with a rack and pinion motion. If *F* be raised, *E* is filled; if *F* be lowered, *E* is emptied. The upper end of *E* divides into two tubes, *g* and *h*, of which *g* is united to *D*. The ascending tube, *h* (gas-delivery tube), is very narrow, and is bent so that its free end dips into a vessel containing mereury, *v* (a pneumatic trough), and the opening is placed exactly under the tube

for collecting the gases, the eudiometer, J, which is also filled with mercury. Where *g* and H unite, there is a two-way stop-cock, which in one position, H, places E in communication with A, B, G, D, the chambers to be exhausted, and in the position K shuts off A, B, G, D, and places the bulb, E, in communication with the gas-delivery tube, *h*, and the eudiometer, J.

B, G, D are completely emptied of air thus:—The stop-cock is placed in the position, K; raise F until drops of mercury issue from the fine tube, *i* (not yet placed under J); place the stop-cock in the position H, lower F; stop-cock in position, K, and so on until the barometer, *y*, indicates a complete vacuum. J is now placed over *i*. Open the cocks, *c* and *b*, so that the blood-bulb, A, communicates with the rest of the apparatus, and the blood gases froth up in B, and after being dried in G pass towards E. Lower F, and they pass into E; stop-cock in position, K, raise F, and the gases are collected in J under mercury. The repeated lowering and raising of F with the corresponding position of the stop-cocks ultimately drives all the gases into J. The removal of the gases is greatly facilitated by placing the blood-bulb, A, in a vessel containing water at 60° C. [Non-defibrinated blood may be used with this pump, and the gases are kept dry by being connected with the chamber, G, containing sulphuric acid.]

It is well to remove the gases from the blood immediately after it is collected from a blood-vessel, because the O undergoes a diminution if the blood be kept. Of course, in making several analyses, it is difficult to do this, and the best plan to pursue in that case is to keep the receptacles containing the blood on ice.

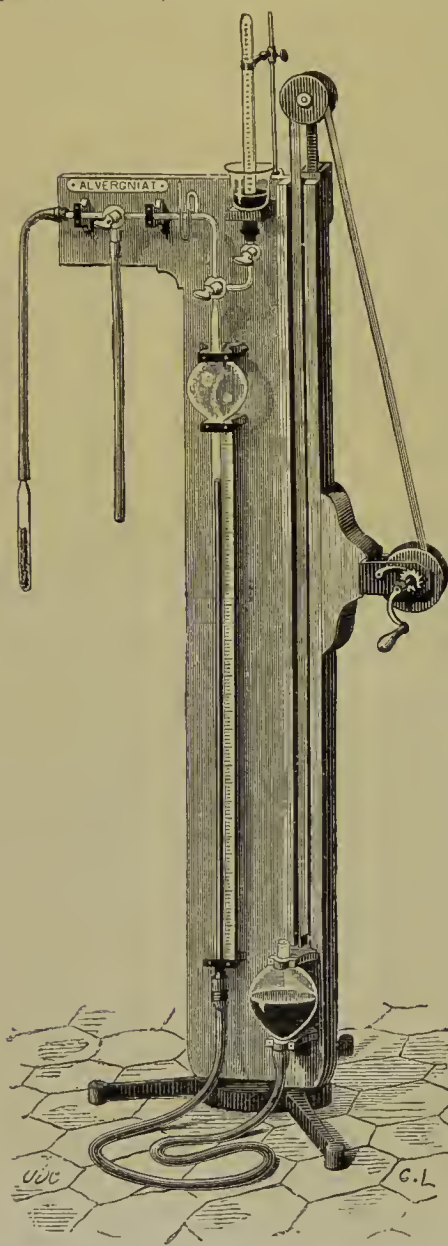
[Alvergriat's Pump.]—A simpler form of gas-pump, first used by Gréhant, modified and used by Paul Bert, and called after its present maker, is frequently adopted (figs. 30 and 31). It is the one most frequently employed in the French laboratories. The receptacle (R) receives the blood from the tube (*t*). The bulbs (A and B), connected by a caoutchouc tube and containing mercury, represent the pump. The bulb (B) can be raised or lowered by means of the handle (M), a flat band being attached to B and working over a pulley (P). By alternately raising and depressing (B), a vacuum is created in the reservoir (R) and the tubes connected with it. The gases pass over into the eudiometer (*h*), which has its lower end in the cup (*c*) containing mercury.]

[The mercury pump (A, B) is composed of a thick, vertically placed barometer tube (*a*) communicating below by thick caoutchouc tubing with the bulb (B) containing Hg. The bulb (A) communicates superiorly by means of the three-way stop-cock (T) with the cup of mercury (*c*), and thus with the eudiometer (*h*), while horizontally it communicates with the tubes connected with the reservoir (R). The stop-cock (T) can be so placed as to cut off all communication between the bulb (A) and the exterior, or the bulb can be placed in communication with *h*, or with R.]

[This is done as follows:—Place the tap (T) in the

Fig. 30.
Gréhaut's and Bert's gas-pump, as made
by Alvergriat of Paris.

position (2), raise B until it is filled with Hg, and all the air is driven out at *b*. Turn the tap into the position (1) so that all connection between A and *g* is cut off; lower B, and a vacuum is established in A and *a*. Place the tap in the position (3), and connect A with *g*, and therefore with R, the tap in *t* being closed, when at once a partial vacuum is established in the system R, *g*, A, *a*. Turn the tap T into the position (2), raise B and expel the air through *b*. Turn the tap T into the position (1), lower B, turn the tap into the position (2), and part of the remainder of the air in *g* and R passes into A and *a*, so that the vacuum in R and *g* is still further increased. Repeat the process as above until a complete vacuum exists in R and *g*. Collect 100 c.c. of blood under mercury, and introduce 50 c.c. of it through the tube *t* into the large receiver R,



when it gives up its gases to the vacuum. The blood immediately froths up and loses its bright red colour, becoming of a dark claret tint. Fill the tube or endiometer (*h*) with mercury and insert it over *b*. By turning the tap *T* into the position (3), on lowering *B* the blood gases pass into *Aa*, on turning the tap into the position (2) and raising *B* the gases are forced into and collected in *h*. The escape of the gases from the blood is greatly facilitated by placing the bulb *R* in warm water as shown in the figure; and, moreover, the escape of watery vapour helps to carry over the gases more rapidly into *Aa*. In some forms of the instrument a drying-vessel containing pumice stone and sulphuric acid is introduced between *R* and *T*. The joints of the apparatus are surrounded with caps of caoutchouc, which are filled with mercury when the apparatus is in use; thus any leakage at a joint is detected at once.]

Mayow (1670) observed that gases were given off from blood *in vacuo*. Magnus (1837) investigated the percentage composition of the blood gases. The more important recent investigations have been made by Lothar Meyer (1857), and by the pupils of C. Ludwig and E. Pflüger.

35. QUANTITATIVE ESTIMATION OF THE BLOOD GASES.

— The gases obtained from blood consist of O , CO_2 , and N . Pflüger obtained (at $0^\circ C$. and 760 mm. Hg pressure) in round numbers about 60 vols. per cent. from the arterial blood of a dog (large artery) and from venous blood (right side of heart). As is shown in figs. 29 (*J*) and 30, the gases are collected in an **endiometer**, *i.e.*, in a narrow tube, closed at one end, and with a very exact scale marked on it, and having two fine platinum wires melted into its upper end, with their free ends projecting into the tube (*p* and *n*).

(1) **Estimation of the CO_2 .**—A small ball of *fused caustic potash*, fixed on a platinum wire, is introduced into the mixture of gases through the lower end of the endiometer under cover of the mercury. The surface of the potash ball is moistened before it is introduced. The CO_2 unites with the potash to form potassium carbonate. The potash bulb is withdrawn after 24 hours. The diminution in volume indicates the amount of CO_2 absorbed.

(2) **Estimation of the O .**—(*a*) Just as in estimating the CO_2 , a ball of *phosphorus* on a platinum wire is introduced into the endiometer; it absorbs the O and forms phosphoric acid. Another plan is to employ a small papier-maché ball saturated with *pyrogallic acid in caustic potash*, which rapidly absorbs O . After the ball is removed, the diminution in volume indicates the quantity of O .

(*b*) The O is most easily and accurately estimated by *exploding it in the endiometer*. Introduce a sufficient quantity of H into the endiometer, and accurately ascertain its volume; an electrical spark is now passed between the wires, *p* and *n*, through the mixture of gases; the O

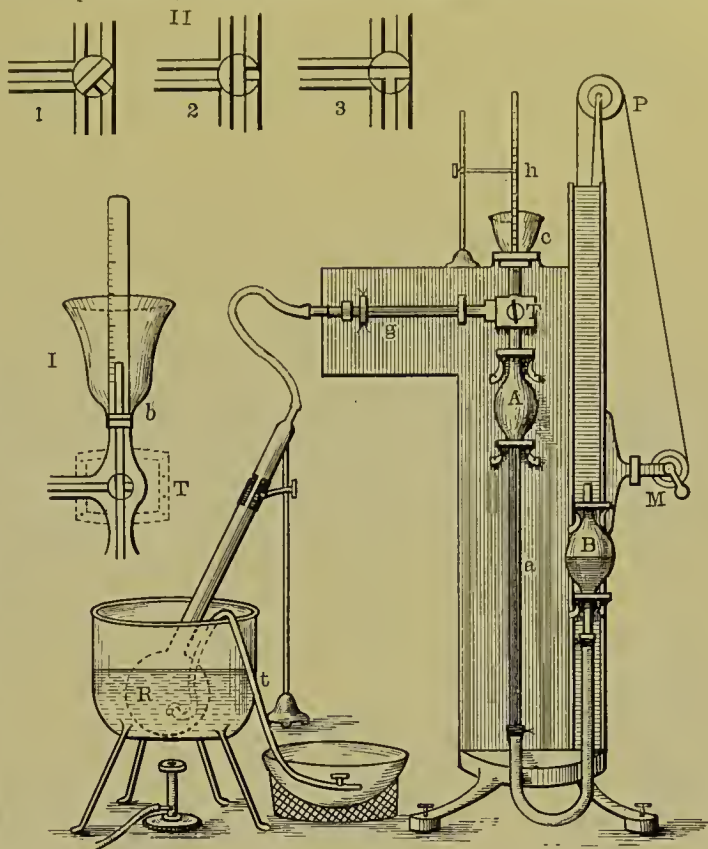


Fig. 31.

Scheme of Alvergniat's gas-pump. *R*, receptacle for blood; *t*, thick tube with tap communicating with it; *A* and *B*, bulbs for mercury; *a*, barometer tubing; *M*, windlass; *P*, pulley; *T*, tap; *g*, connecting-tube to *R*; *c*, cup for mercury; *h*, endiometer; *II*, 1, 2, 3, positions that can be given to the three-way stop-cock or tap *T*. *I*, Small part of *c* and *T* enlarged to show the endiometer.

and H unite to form water, which causes a diminution in the volume of the gases in the eudiometer, of which $\frac{1}{3}$ is due to the O used to form water (H_2O).

(c) **Estimation of the N.**—When the CO_2 and O are estimated by the above method, the remainder is pure N.

36. THE BLOOD GASES.—[In human blood the average total gases are estimated to be in round numbers 60 vols. per cent. at 0° C. and 760 mm. pressure, made up as follows:—

	O	CO_2	N
Arterial blood,	20	39	1.4 per cent.
Venous blood,	8 to 12	46	1.4 „]

or, 47.3 vols. per cent. calculated at 0° C. and 1 metre pressure,

	O	CO_2	N
Arterial blood,	17	30	1 to 2 per cent.
Venous blood,	6 to 10	35	1 to 2 „

[Thus venous blood contains 8–12 per cent. less O and 6 per cent. more CO_2 than arterial blood. The amount of gases obtained from venous blood under different conditions varies greatly, as is stated below.]

I. **Oxygen** exists in **arterial** blood (dog) on an average to the extent of 17 volumes per cent. (at 0° C. and 1 metre Hg. pressure) (*Pflüger*), or 20 volumes per cent. (at 0° C. and 760 mm. pressure). According to *Pflüger*, arterial blood (dog) is saturated to $\frac{9}{10}$ with O, while, according to *Hüfner*, it is saturated to the extent of $\frac{1.4}{1.5}$. In **venous** blood the quantity varies very greatly; in the blood of a passive muscle 6 volumes per cent. have been found; while in the blood after asphyxia it is absent, or occurs only in traces. It is certainly more abundant in the comparatively red blood of active glands (salivary glands, kidney) than in ordinary dark venous blood.

[**Modifying Conditions.**—The amount of O obtainable from the blood depends upon the organ from which the blood comes, or whether the organ be active or at rest. Thus the O present in the

Carotid artery is . . .	21 per cent.		Renal vein (kidney active), 17 per cent.
Renal artery, . . .	19 „		Renal vein (kidney at rest), 6 „

Bert finds that increase of the atmospheric pressure from 1 to 10 atmospheres raises the amount of O in arterial blood from 20 to over 24 per cent., and the N from 1.8 to over 9 per cent., while the CO_2 is but slightly affected. Only 10–15 volumes per cent. of O are obtained from the blood of herbivora (sheep, rabbit), as these animals have a small number of corpuscles, and hæmoglobin. The amount of hæmoglobin and O is much less in cold-blooded animals. The amount of CO_2 in peptone blood is diminished by about one-half, while the O is slightly increased (*Lahousse*).]

The O in Blood occurs—(a) *simply absorbed* in the plasma. This is only a minimal amount, and does not exceed what distilled water at the temperature of the body would take up at the partial pressure of the O in the air of the lungs (*Lothar Meyer*).

(b) *Almost the total O of the blood is chemically united*, and therefore not subject to the law of absorption. It is *loosely* united to the hæmoglobin of the red corpuscles, with which it forms **oxyhæmoglobin** (§ 15). With regard to the taking up of O, the total quantity of blood behaves exactly like a solution of hæmoglobin free from O (*Preyer*). The absorption of O is more rapid in blood than in a solution of Hb.

The absorption of this quantity of O is completely **independent of pressure**; hence, animals confined in a close space, until they are nearly asphyxiated, can use up almost all the O from the surrounding atmosphere. The fact of the union being independent of pressure is proved by the following:—The blood only gives off copiously its chemically united O when the atmospheric pressure is lowered to 20 millimetres Hg, (*Worm Müller*); and, conversely, blood only takes up a little more O when the pressure is increased to 6 atmospheres (*Bert*).

Physical Methods of obtaining O from Blood.—Notwithstanding the chemical

union between the Hb and O, all the O of the blood can be expelled from its state of combination by those means which set free absorbed gases—

(a) by introducing blood into a Torricellian vacuum.

(b) by boiling.

(c) by the conduction of other gases [H, N, CO, or NO] through the blood, because the oxyhæmoglobin compound is so loose that it is decomposed even by these physical means.

Reducing Reagents.—Amongst *chemical* reagents the following *reducing* substances—ammonium sulphide, sulphuretted hydrogen, alkaline solutions of salts or Stokes's fluid, iron filings, &c., rob blood of its O (§ 15).

Relation to Fe.—The amount of iron in the blood (0.55 in 1000 parts) stands in direct relation to the amount of Hb; this to the quantity of blood-corpuscles; and this, in turn, to the specific gravity of the blood. The amount of O in the blood, therefore, is nearly proportional to the specific gravity of the blood, and it is also in proportion to the amount of iron in the blood. The total amount of iron in the blood is about 3 grams.

During morphia narcosis the amount of O in the blood is diminished (*Ewald*); after hæmorrhage the arterial blood is saturated with O (*J. G. Ott*).

Disappearance of O in Shed Blood.—Even immediately after blood is shed there is a slight disappearance of O, as a physiological index of respiration of the tissues within the living blood itself (§ 131). When blood is kept long outside of the blood-vessels, the quantity of O gradually diminishes, and if it be kept for a length of time at a high temperature it may disappear altogether. This depends upon decomposition occurring in the blood, whereby reducing substances are formed which consume the O. All kinds of blood, however, do not act with equal energy in consuming O, *e.g.*, venous blood from active muscles acts most energetically, while that from the hepatic vein has very little effect. CO₂ appears in the blood in place of the O, and the colour darkens. The amount of CO₂ produced is sometimes greater than that of the O consumed.

Relation to Acids.—If blood (or a solution of oxyhæmoglobin) be acted upon by *acids* (*e.g.*, tartaric acid) until it is strongly acid, O can be pumped out in considerably less amount, while the formation of CO₂ is not increased. We must therefore assume that, during the decomposition of the Hb caused by the acids (§ 18), a decomposition product becomes more highly oxidised by the intense chemical union of the O at the moment of its origin (*Lothar Meyer, Zuntz, Strassburg*). The same phenomenon occurs when oxyhæmoglobin is decomposed by *boiling*.

37. IS OZONE PRESENT IN BLOOD?—On account of the numerous and energetic oxidations which occur in connection with the blood, the question has often been raised as to whether the O of the blood exists in the form of ozone (O₃). Ozone, however, is contained neither in the blood itself (*Schönbein*) nor in the blood gases obtained from it. Nevertheless, the red corpuscles (and Hb) have a distinct relation to ozone.

(1) **Tests for Ozone.**—Hæmoglobin acts as a *conveyer of ozone*, *i.e.*, it is able to remove the active O of other bodies and to *convey* or transfer it at once to other easily oxidisable substances. (a) Turpentine which has been exposed to the air for a long time always contains ozone. The tests for the latter are starch and potassium iodide, the ozone decomposing the iodide, when the iodine strikes a blue with the starch. (b) Freshly-prepared tincture of guaiacum is also rendered blue by ozone. If some tincture of guaiacum be added to turpentine there is no reaction, but on adding a drop of blood a deep blue colour is immediately produced, *i.e.*, blood takes the ozone from the turpentine and *conveys* it at once to the dissolved guaiacum, which becomes blue. It is immaterial whether the Hb contains O or not.

(2) It is also asserted that hæmoglobin acts as an *ozone-producer*, *i.e.*, that it can convert the ordinary O of the air into ozone. Hence the reason why red blood-corpuscles alone render guaiacum blue. This reaction succeeds best when the guaiacum solution is allowed to dry on blotting-paper, and a few drops of blood (diluted 5 to 10 times) are poured on it. That the Hb forms ozone from the surrounding O is shown by the fact that red blood-corpuscles containing carbonic oxide cause the blue colour (*Kühne and Scholz*). According to Pflüger, however, these reactions only occur from decomposition of the Hb, so that on this view the blood-corpuscles cannot be regarded as producers of ozone.

Sulphuretted hydrogen is decomposed by blood (as by ozone itself) into sulphur and water. Hydric peroxide is decomposed by blood into O and water [but this reaction is prevented by the addition of a small amount of hydrocyanic acid (*Schönbein*)]. Crystallised Hb does not do this, and H₂O₂ may be cautiously injected into the blood-vessels of animals. This would show that *unchanged* Hb does not produce ozone.

Various Forms of Oxygen.—There are three forms of oxygen :—(1) The ordinary oxygen (O₂)

in the air. (2) Active or nascent oxygen (O), which never can occur in the free state, but the moment it is formed acts as a powerful oxidising agent and produces chemical compounds. It converts water into hydric peroxide—the N of the air into nitrous and nitric acids, and even CO into CO_2 , which ozone does not. It certainly plays an important part in the organism. (3) Ozone (O_3), which is formed by the decomposition of several molecules of ordinary oxygen (O_2) into two atoms of O, and the appropriation of each of these atoms by a molecule of undecomposed oxygen. It is oxygen condensed to $\frac{2}{3}$ of its volume.

38. CO_2 AND N IN BLOOD.—II. **Carbon Dioxide.**—In arterial blood there are about 39 volumes per cent. at 0°C . and 760 mm. Hg pressure or 30 volumes per cent. of CO_2 at 0°C . and 1 metre pressure (*Setschenow*); but in venous blood the amount is very variable, e.g., in the venous blood of passive muscles there are 35 volumes per cent. (*Sczelkow*), while in the blood of asphyxia there may be 52.6 volumes per cent. The CO_2 in the lymph of asphyxia is less than that in the blood (*Buchner, Gaule*). The CO_2 of the blood may be extracted from it or completely pumped out, without, however, the alkaline reaction of the blood undergoing any change (*Zuntz*).

(A) **The CO_2 in Plasma (or Serum).**

(a) A minimal part is simply absorbed by the fluid part of the blood.

(b) The largest portion of the CO_2 belongs to the plasma (or serum), and it all appears to be in a state of chemical combination. Serum takes up CO_2 quite independently of pressure, hence it cannot be merely absorbed. The CO_2 may exist in the following combinations:—

(1) A portion of the CO_2 is loosely united to sodic carbonate in the form of *sodic bicarbonate*; the carbonate takes up 1 equivalent of CO_2 ; $\text{Na}_2\text{CO}_3 + \text{CO}_2 + \text{H}_2\text{O} = 2\text{NaHCO}_3$. This CO_2 may be pumped out, as in the process the bicarbonate splits up again into the neutral carbonate and CO_2 .

(2) As the bicarbonate only gives up its CO_2 very slowly *in vacuo*, while blood gives off its CO_2 very energetically, perhaps the soda, united with an albuminous body (serum-globulin-alkali [*Torup*]) combines with the CO_2 and forms a complex compound, from which the CO_2 is rapidly given off *in vacuo*.

(3) A minimal portion of the CO_2 may be chemically united with *neutral sodic phosphate* in the plasma (*Fernet*). One equivalent of this salt can fix one equivalent of CO_2 , so acid sodium phosphate and acid sodium carbonate are formed, $\text{Na}_2\text{HPO}_4 + \text{CO}_2 + \text{H}_2\text{O} = \text{NaH}_2\text{PO}_4 + \text{NaHCO}_3$ (*Hermann*). When the gases are removed the CO_2 escapes, and neutral sodic phosphate remains.

It is probable, however, that almost all the sodic phosphate found in the blood-ash arises from the burning of lecithin; we have, therefore, to consider only the very small amount of this salt which occurs in the plasma (*Hoppe-Seyler and Sertoli*).

(B) **The CO_2 in the Blood-Corpuscles.**

The red corpuscles contain CO_2 in loose chemical combination; for (1) a volume of blood can fix nearly as much CO_2 as an equal volume of serum (*Ludwig, Al. Schmidt*); and (2) with increasing pressure the absorption of CO_2 by blood takes place in a different ratio from what occurs with serum (*Pflüger, Zuntz*). The red corpuscles can fix more CO_2 than their own volume, and the union of the CO_2 seems to depend upon the Hb, for *Setschenow* found that, when Hb was acted on by CO_2 , its power of fixing the latter was increased, which is perhaps due to the formation of some substance more suited for fixing CO_2 . *Bohr* found that 1 gram of dissolved Hb (dog) at 120 mm. Hg pressure unites with 3.5 c.e. CO_2 , i.e., more than double the quantity of O absorbed (p. 25). It seems also to be partly united to the globulin-alkali compound (*Bohr, Torup*). The leucocytes, after the manner of the serum-constituents, also fix CO_2 to the extent of $\frac{1}{3}$ to $\frac{1}{12}$ of the absorbing power of serum.

After the use of I, Hg, sodic oxalate, and nitrite, there is a diminution of CO_2 in arterial blood (*Feitelberg*), and also in fever (*Geppert, Minkowski*). [In the last case it is perhaps due

to the diminished alkalinity, and this is in part owing to the acid products formed during the decomposition of the tissues.]

III. **Nitrogen** exists in the blood to the extent of 1.4 to 1.6 vol. per cent., and it appears to be simply **absorbed**.

It is doubtful if any part of the N exists chemically united in the red corpuscles. Blood warmed outside the body, and with a free supply of oxygen, gives off a minute quantity of ammonia, which is perhaps derived from the decomposition of some salt of ammonia as yet unknown (*Kühne and Strauch*).

39. ARTERIAL AND VENOUS BLOOD.—Arterial blood contains in solution all those substances which are necessary for the nutrition of the tissues, those which are employed in secretion, and it also contains a rich supply of O, and, as we have seen, a considerable amount of CO₂. **Venous blood** contains less of the nutrient matter, but in addition it holds the used-up or effete substances derived from the tissues, and the products of their retrogressive metabolism are more numerous; there is in venous blood a larger amount of CO₂, and also a considerable amount of O.

[The fundamental difference between Arterial and Venous blood is due to the relative proportion of oxygen and carbon dioxide contained in each. The difference in colour depends on this. If venous blood be shaken up with air or oxygen it becomes arterial, while if arterial blood be submitted to a current of an indifferent gas such as N or H, it becomes venous. It also does so if it be sealed up in a vessel for some time, whereby the oxygen is used up, and gradually more and more of the oxyhæmoglobin is changed into reduced hæmoglobin.]

It is evident also that the blood of certain veins, the portal and hepatic, must have special characters.

The following are the most important points of difference between arterial blood and venous blood:—

Arterial Blood contains—		
more O,	more salts,	It is redder and not dichroic. As a rule it is 1° C. warmer. It coagulates more rapidly.
less CO,	more fat,	
more water,	more sugar,	
more fibrin,	fewer blood-corpuscles,	
more extractives,	less urea.	

The **bright red** colour of arterial blood depends on the presence of oxyhæmoglobin, whilst the dark colour of venous blood is due to its smaller proportion of oxyhæmoglobin, and the quantity of reduced hæmoglobin which it contains. The dark change of colour is not to be attributed to the larger quantity of CO₂ in venous blood (*Marchand*); for if equal quantities of O be added to two portions of blood, and if CO₂ be added to one of them, the colour is not changed (*Pflüger*).

[According to C. Schmidt, the blood of the **portal vein** contains more water, plasma, salts, and fats, but less extractives and corpuscles than the blood of the hepatic vein; while (when an animal is not digesting) sugar is absent, or at least only in traces in the portal vein, and in considerable amount in the hepatic vein (§ 175).]

[Blood of the **hepatic vein** is said to contain more corpuscles than that of the portal vein, and it is supposed not to coagulate after death, but this is very doubtful. According to Drosdoff, it contains more water, cholesterin, and lecithin than the portal vein except during digestion; it also contains more sugar, and it is the warmest blood in the body.]

[**Splenic Vein.**—Some observers say that this vein contains more, and others fewer, red blood-corpuscles than that of the artery. The statement is also made that it contains more white corpuscles, but this, again, is denied by Tarchanoff. The notion that its serum contains hæmoglobin has been disproved by Schäfer. In this latter respect it does not differ from that of serum of blood generally.]

[**Renal Vein.**—Here the blood is bright red, and holds more O and less CO₂ than the blood of the renal artery. It contains less water, NaCl, uric acid, and urea, and coagulates with difficulty.]

40. QUANTITY OF BLOOD.—In the **adult** the quantity of blood is equal to $\frac{1}{13}$ part of the body-weight (*Bischoff*), [*i.e.* on an average 4–4·5 kilos (8·8–9·9 lbs.)]; in newly-born children $\frac{1}{9}$ (*Welcker*).

According to Schücking, the amount of blood in a **newly-born child** depends to some extent upon the time at which the umbilical cord is ligatured. The amount = $\frac{1}{15}$ of the body-weight when the cord is tied at once, while if it is tied somewhat later it may be $\frac{1}{6}$. Immediate ligature of the cord may, therefore, deprive a newly-born child of 100 grams of blood. Further, the number of corpuscles is less in a child after immediate ligature of the umbilical cord than when it is tied somewhat later (*Helot*).

The methods of Valentin (1838), and Ed. Weber (1850), are not now used, as the results obtained are not sufficiently accurate.

Method of Welcker (1854).—Begin by taking the weight of the animal to be experimented on; place a cannula in the carotid, and allow the blood to run into a flask previously weighed, and in which small pebbles (or Hg) have been placed, in order to defibrinate the blood by shaking. Take a part of this defibrinated blood, and make it cherry-red in colour by passing through it a stream of CO (because ordinary blood varies in colour according to the amount of O contained in it—*Gscheidlen, Heidenhain*). Tie a $\perp$ shaped cannula in the two cut ends of the carotid, and allow a 0·6 per cent. solution of common salt to flow into the vessel from a pressure bottle; collect the coloured fluid issuing from the jugular veins and inferior vena cava until the fluid is quite clear. The entire body is then chopped up (with the exception of the contents of the stomach and intestines, which are weighed, and their weight deducted from the body-weight), and extracted with water, and after twenty-four hours the fluid is expressed. This water, as well as the washings with salt solution, are collected and weighed, and part of the mixture is saturated with CO. A sample of this dilute blood is placed in a vessel with parallel sides (1 cm. apart) opposite the light (the so-called hæmatinometer), and in a second vessel of the same dimensions a sample of the undiluted CO blood is diluted with water from a burette, until both fluids give the *same intensity of colour*. From the quantity of water required to dilute the blood to the tint of the washings of the blood-vessels, the quantity of blood in the washings is calculated. On chopping up the muscles alone, we obtain the amount of Hb present in them, which is not taken into calculation.

Quantity of Blood in Various Animals.—The quantity of blood in the mouse = $\frac{1}{12}$ to $\frac{1}{13}$; guinea-pig = $\frac{1}{10}$ ·7 ($\frac{1}{17}$ to $\frac{1}{22}$); rabbit = $\frac{1}{20}$ ($\frac{1}{15}$ to $\frac{1}{22}$); dog = $\frac{1}{13}$ ($\frac{1}{11}$ to $\frac{1}{18}$); cat = $\frac{1}{21}$ ·5; birds = $\frac{1}{10}$ to $\frac{1}{13}$; frog = $\frac{1}{15}$ to $\frac{1}{20}$; fishes = $\frac{1}{14}$ to $\frac{1}{19}$ of the body-weight (without the contents of the stomach and intestines).

The specific gravity of the blood ought always to be taken when estimating the amount of blood. The amount of blood is diminished during inanition; fat persons have relatively less blood; after hæmorrhage the loss is at first replaced by a watery fluid, while the blood-corpuscles are gradually regenerated.

The estimation of the **quantity of blood in different organs** is done by suddenly ligaturing their blood-vessels *intra vitam*. A watery extract of the chopped-up organ is prepared, and the quantity of blood estimated as described above. [Roughly it may be said that the lungs, heart, large arteries, and veins contain $\frac{1}{4}$; the muscles of the skeleton, $\frac{1}{4}$; the liver, $\frac{1}{4}$; and other organs, $\frac{1}{4}$ (*Ranke*).]

[Fate of Salts injected into the blood-stream.—One of the most noteworthy facts about the composition of the blood is the remarkable constancy in the proportion of its chemical constituents, and this is specially true of its salts. It is impossible to render blood acid by giving animals repeated doses of acid, and when salts are administered in excess, the blood rapidly gets rid of them. If salts (Na_2SO_4 , Na_2HPO_4 , NaCl) be injected into the blood-vessels, the salts immediately diffuse into the tissues, so that within a few minutes only traces can be recovered from the blood. At the same time the tissues give up water to the blood, and gradually the salts re-enter the blood and are given off by the kidneys.]

41. ABNORMAL CONDITIONS OF THE BLOOD.—(A) 1. **Polyæmia.**—(1) An increase in the entire mass of the blood, *uniformly in all organs*, constitutes *polyæmia* or *plethora*, and in over-nourished individuals it may approach a pathological condition. A bluish-red colour of the skin, swollen veins, large arteries, hard full pulse, injection of the capillaries and smaller vessels of the visible mucous membranes are signs of this state, and, when accompanied by congestion of the brain, there is vertigo, congestion of the lungs, and breathlessness. After major amputations with little loss of blood, a relative but transient increase of blood has been found (?) (*plethora apocoptica*).

Transfusion.—Polyæmia may be produced artificially by the *injection of blood* of the same

species. If the normal quantity of blood be increased 83 per cent. no abnormal condition occurs, because the blood-pressure is not permanently raised. The excess of blood is accommodated in the greatly distended capillaries, which may be stretched beyond their normal elasticity. If it be increased to 150 per cent. there are variations in the blood-pressure, life is endangered, and there may be sudden rupture of blood-vessels (*Worm Müller*).

Fate of Transfused Blood.—After the transfusion of blood the formation of lymph is greatly increased; but in one or two days the serum is used up, the water is excreted chiefly by the urine, and the albumin is partly changed into urea. Hence, the blood at this time appears to be relatively richer in blood-corpuscles (*Pannum, Lesser, Worm Müller*). The red corpuscles break up much more slowly, and the products thereof are partly excreted as urea and partly (but not constantly) as bile-pigments. Even after a month an increase of coloured blood-corpuscles has been observed (*Tschirjew*). That the blood-corpuscles are broken up *slowly* in the economy is proved by the fact, that the amount of urea is much larger when the same quantity of blood is swallowed by the animal than when an equal amount is transfused (*Tschirjew, Landois*). In the latter case there is a moderate increase of the urea, lasting for days, a proof of the slow decomposition of the red corpuscles. Pronounced over-filling of the vessels causes loss of appetite and a tendency to hæmorrhage of the mucous membranes.

(2) **Polyæmia serosa** is that condition in which the amount of serum, *i.e.*, the amount of water in the blood, is increased. This may be produced artificially by the transfusion of blood-serum from the same species. The water is soon given off in the urine, and the albumin is decomposed into urea, without, however, passing into the urine. An animal forms more urea in a short time from a quantity of transfused serum than from the same quantity of blood, a proof that the blood-corpuscles remain longer undecomposed than the serum (*Forster, Landois*). If serum from another species of animal be used (*e.g.*, dog's serum transfused into a rabbit), the blood-corpuscles of the recipient are dissolved; hæmoglobinuria is produced (*Ponfick*); and if there be general dissolution of the corpuscles, death may occur (*Landois*).

(3) **Polyæmia aquosa** is a simple increase of the water of the blood, and occurs temporarily after copious drinking, but increased diuresis soon restores the normal condition. Diseases of the kidneys, which destroy their secreting parenchyma, produce this condition, and often also general dropsy, owing to the passage of water into the tissues. Ligature of the ureter produces a watery condition of the blood.

(4) **Plethora polycythæmica, Hyperglobulie.**—An increase of the red corpuscles has been assumed to occur when periodically recurring hæmorrhages are interrupted, *e.g.*, menstruation, bleeding from the nose, &c.; but the increase of corpuscles has not been definitely proved. There is a proved case of temporary polycythæmia, *viz.*, when similar blood is transfused, a part of the fluid being used up, while the corpuscles remain unchanged for a considerable time. There is a remarkable increase in the number of blood-corpuscles (to 8·82 millions per cubic millimetre) in certain severe cardiac affections where there is great congestion, and much water transudes through the vessels. In cases of hemiplegia, for the same reason, the number of corpuscles is greater on the paralysed congested side (*Pensoldt*). After diarrhœa, which diminishes the water of the blood, there is also an increase (*Brouardel*), and the same is the case after profuse sweating and polyuria. Drugs (alcohol, chloral, amyl nitrite) which act on the blood-vessels affect the number of corpuscles; during contraction of the blood-vessels their number increases, during dilatation they diminish in number (*Andreesen*). There is a temporary increase in the hæmatoblasts as a reparative process after severe hæmorrhage (§ 7), or after acute diseases. In cachectic conditions this increase continues, owing to the diminished non-conversion of these corpuscles into red corpuscles. In the last stages of cachexia the number diminishes more and more until the formation of hæmatoblasts ceases (*Hayem*).

(5) **Plethora hyperalbuminosa** is a term applied to the increase of albumins in the plasma, such as occurs after taking a large amount of food. A similar condition is produced by transfusing the serum of the same species, whereby, at the same time, the urea is increased. Injection of egg-albumin produces albuminuria (*Stokvis, Lehmann*).

[The **subcutaneous injection** of human blood has been practised with good results in anæmia (*v. Ziemssen*). When defibrinated human blood is injected subcutaneously, while its passage into the circulation is aided by massage, it causes neither pain nor inflammation, but the blood of animals, and a solution of hæmoglobin, always induce abscess (*Benecur*). Blood is also rapidly absorbed when injected in small amount into the respiratory passages.]

Mellitæmia.—The sugar in the blood is partly given off by the urine, and in “diabetes mellitus” 1 kilo. (2·2 lbs.) may be given off daily, when the quantity of urine may rise to 25 kilos. To replace this loss of grape-sugar a large amount of food and drink is required, whereby the urea may be increased threefold. The increased production of sugar causes an increased decomposition of albuminous tissues; hence the urea is always increased, even though the supply of albumin be insufficient. The patient loses flesh; all the glands, and even the testicles, atrophy or degenerate (pulmonary phthisis is common); the skin and bones become thinner; the nervous system holds out longest. The teeth become carious on account of the acid saliva, the crystalline lens becomes turbid from the amount of sugar in the fluid of the eye which extracts water from the lens, and wounds heal badly because of the abnormal condition of the blood.

Absence of all carbohydrates in the food causes a diminution of the sugar in the blood, but does not cause it to disappear entirely. [The sugar in the blood is also increased after the inhalation of chloroform or amyl nitrite, and after the use of eura, nitro-benzole, and chloral (§ 175).] An excessive amount of inosite has been found in the blood and urine (§ 267), constituting *mellituria inosita* (Vohl).

Lipæmia, or an increase of the Fat in the Blood, occurs after every meal rich in fat (*e.g.*, in sucking kittens), so that the serum may become turbid like milk. Pathologically, this occurs in a high degree in drunkards and in corpulent individuals. When there is great decomposition of albumin in the body (and therefore in very severe diseases), the fat in the blood increases, and this also takes place after a liberal supply of easily decomposable carbohydrates and much fat.

After injuries to bones affecting the marrow, not unfrequently fatty granules pass from the marrow through the imperfect walls of the blood-vessels into the blood-stream. These fatty particles may form fat emboli, *e.g.*, in the liver or lungs, or they may appear in the urine.

If granules of einnabar or indigo are injected into the blood, they are taken up by the leucocytes, and by them are carried outside the blood-stream. The cells of the splenic pulp, marrow of bone, and the liver also take up these particles (*Siebel*).

The salts remain very persistently in the blood. The withdrawal of common salt produces albuminuria, and, if all salts be withheld, paralytic phenomena occur (*Forster*). Over-feeding with salted food, such as salt meat, has caused death through fatty degeneration of the tissues, especially of the glands. Withdrawal of lime and phosphoric acid produces atrophy and softening of the bones. In infectious diseases and dropsies the salts of the blood are often increased, and diminished in inflammation and cholera. [NaCl is absent from the urine in certain stages of pneumonia, and it is a good sign when the chlorides begin to return to the urine.] [In scurvy the corpuscular elements are diminished in amount, but we have not precise information as to the salts, although this disease is prevented, in persons forced to live upon preserved and salted food, by a liberal use of the salts—especially potash salts—of the organic acids, as contained in lime-juice. In gout, the blood during an acute attack, and also in chronic gout, contains an excess of uric acid (*Garrod*).]

The amount of fibrin is increased in inflammations of the lung and pleura, [serpious pneumonia, erysipelas], hence such blood forms a *crusta phlogistica* (§ 27). In other diseases, where decomposition of the blood-corpuscles occurs, the fibrin is increased, perhaps because the dissolved red corpuscles yield material for the formation of fibrin. After repeated hæmorrhages, Sign. Mayer found an increase of fibrin. Blood rich in fibrin is said to coagulate *more slowly* than when less fibrin is present—still there are many exceptions.

(B) (I.) **Diminution of the Quantity of Blood, or its Individual Constituents.**—(1) **Oligæmia vera, Anæmia**, or diminution of the quantity of blood as a whole, occurs whenever there is hæmorrhage. Life is endangered in newly born children when they lose a few ounces of blood; in children a year old, on losing half a pound; and in adults, when one-half of the total blood is lost. Women bear loss of blood much better than men. The periodical formation of blood after each menstruation seems to enable blood to be renewed more rapidly in their case. Stout persons, old people, and children do not bear the loss of blood well. The more rapidly blood is lost, the more dangerous it is. [A moderate loss of blood is soon made up, but the fluid part is more quickly restored than are the corpuscles.]

Symptoms of Loss of Blood.—Great loss of blood is accompanied by general paleness and coldness of the cutaneous surface, increased oppression, twitching of the eyeballs, noises in the ears and vertigo, loss of voice, great breathlessness, stoppage of secretions, coma; dilatation of the pupils, involuntary evacuations of urine and feces, and lastly, general convulsions, are sure signs of death by hæmorrhage. In the gravest cases recovery is only possible by means of transfusion. Animals can bear the loss of one-fourth of their entire blood without the blood-pressure in the arteries permanently falling, because the blood-vessels contract and accommodate themselves to the smaller quantity of blood (in consequence of the stimulation of the vasomotor centre in the medulla). The loss of one-third of the total blood diminishes the blood-pressure considerably (one-fourth in the carotid of the dog). If the hæmorrhage is not such as to cause death, the fluid part of the blood and the dissolved salts are restored by absorption from the tissues, the blood-pressure gradually rises, and then the albumin is restored, though a longer time is required for the formation of red corpuscles. At first, therefore, the blood is abnormally rich in water (*hydræmia*), and at last abnormally poor in corpuscles (*oligocythæmia*, *hypoglobulie*). With the increased lymph-stream which pours into the blood, the colourless corpuscles are considerably increased above normal, and during the period of restitution fewer red corpuscles seem to be used up (*e.g.*, for bile).

After moderate bleeding from an artery in animals, Buntzen observed that the volume of the blood was restored in several hours; after more severe hæmorrhage in 24 to 48 hours. The red blood-corpuscles, after a loss of blood equal to 1.1 to 4.4 per cent. of the body-weight, are restored only after 7 to 34 days. The regeneration begins after 24 hours. During the period of regeneration the number of the blood-corpuscles in an early stage of development is increased. The newly-formed corpuscles contain less Hb than normal (*Jac. G. Ott*). Even in man the

duration of the period of regeneration depends upon the amount of blood lost (*Lyon*). The amount of hæmoglobin is diminished nearly in proportion to the amount of the hæmorrhage (*Bizzozero and Salvioli*).

[**Hæmorrhages in cold-blooded animals.**—These animals can bear very considerable loss of blood, and, in fact, the frog can live for a considerable time without blood. In the experiment of Cohnheim known as the “salt frog,” all the blood is washed out of its vessels by means of normal saline solution (75 per cent. NaCl) and the blood-vessels are filled with the same fluid. Such a frog will live for several days, and the elimination of CO_2 goes on as in an intact frog. This experiment obviously has a very important bearing on the question as to the seat of the formation of CO_2 —*i.e.*, whether it is formed in the blood or in the tissues. It clearly points to the latter view.]

Metabolism in Anæmia.—The condition of the metabolism in the case of persons suffering from anæmia is important. The decomposition of proteids is increased (the same is the case in hunger), hence the excretion of urea is increased (*Bauer*). The decomposition of fats, on the contrary, is diminished, which stands in relation with the diminution of CO_2 given off. Anæmic and chlorotic persons put on fat easily. The fattening of cattle is aided by occasional bleedings and by intercurrent periods of hunger (*Aristotle*).

(2) An excessive thickening of the blood through loss of water is called *Oligæmia sicca*. This occurs in man after copious watery evacuations, as in cholera, so that the thick tarry blood stagnates in the vessels. Perhaps a similar condition—though to a less degree—may exist after very copious perspiration.

(3) If the proteids in blood be abnormally diminished the condition is called *Oligæmia hypalbuminosa*; they may be diminished about one-half. They are usually replaced by an excess of water in the blood [so that the blood is watery, constituting *hydræmia*]. Loss of albumin from the blood is caused directly by albuminuria (25 grams of albumin may be given off by the urine daily), persistent suppuration, great loss of milk, extensive cutaneous ulceration, albuminous diarrhœa (dysentery). Frequent and copious hæmorrhages, however, by increasing the absorption of water into the vessels, at first produces oligæmia hypalbuminosa.

For the abnormal changes of the red and white blood-corpuscles, see § 10; for *Hæmophilia*, § 28.

[**Organisms in the Blood.**—The presence of animal and vegetable parasites in the blood gives rise to certain diseases. Some of these, and especially the vegetable organisms, have the power of multiplying in the blood. The vegetable forms belonging to the *schizomycetes* or fission fungi are frequently spoken of collectively under the title *bacteria*. They are classified by Cohn into

- | | |
|---------------------|----------------------|
| I. Sphærobacteria | } exhibit movements. |
| II. Microbacteria | |
| III. Desinobacteria | |
| IV. Spirobacteria | |

These forms are shown in fig. 32. The micrococci (A) are examples of I.; while *Bacterium termo* (B) is an example of II. In III. the members are short cylindrical rods, straight (*Bacillus*, D) or wavy (*Vibrio*, C). Splenic fever of cattle is due to the presence of *Bacillus anthracis* (fig. 32). These rod-shaped bodies under proper conditions divide transversely and elongate, but they also form spores in their interior, which in turn under appropriate conditions may germinate. Class IV. is represented by two genera, *Spirochæta* and *Spirillum* (fig. 32), the former with close, and the latter with open spirals. The *Spirochæta Obermeieri* (often spoken off as “spirillum”) is present in the blood during the paroxysms in persons suffering from relapsing fever. Amongst animal parasites are *Filaria sanguinis*, and *Bilharzia hæmatobia*, which occurs in the portal vein and in the veins of the urinary apparatus.]

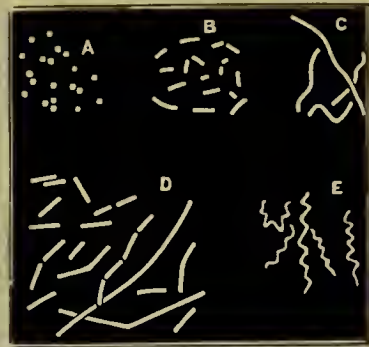


Fig. 32.

A, micrococcus; B, bacterium; C, vibrios; D, bacilli; E, spirillum.

Physiology of the Circulation.

42. GENERAL VIEW.—The blood within the vessels is in a state of continual motion, being carried *from* the ventricles by the large arteries (aorta and pulmonary) and their branches *to* the system of *capillary* vessels, *from* which again it passes into the *veins* that end in the atria of the auricles (*W. Harvey, 1628*).

The **cause of the circulation** is the DIFFERENCE OF PRESSURE which exists between the blood in the aorta and pulmonary artery on the one hand, and the two venæ cavæ and the four pulmonary veins on the other. The blood, of course, moves continually in its closed tubular system in the direction of least resistance. The greater the difference of pressure, the more rapid the movement will be. The cessation of the difference of pressure (as after death) naturally brings the movement to a standstill (§ 81). The circulation is usually divided into—

(1) **The greater, or systemic circulation**, which includes the course of the blood from the left auricle and left ventricle, through the aorta and all its branches, the capillaries of the body and the veins, until the two venæ cavæ terminate in the right auricle.

(2) **The lesser, or pulmonic circulation**, which includes the course from the right auricle and right ventricle, the pulmonary artery, the pulmonary capillaries, and the pulmonary veins springing from them, until these open into the left auricle.

(3) **The portal circulation** is sometimes spoken of as a special circulatory system, although it represents only a second set of capillaries (within the liver) introduced into the course of a venous trunk. It consists of the vena portarum—formed by the union of the intestinal or mesenteric and splenic veins, and it passes into the liver, where it divides into capillaries, from which the hepatic veins arise. The hepatic vein joins the inferior vena cava.

Strictly speaking, however, there is no special portal circulation. Similar arrangements occur in other animals in different organs, *e.g.*, snakes have such a system in their supra-renal capsules, and the frog in its kidneys. When an *artery* splits up into fine branches during its course, and these branches do not form capillaries, but reunite into an arterial trunk, a *rete mirabile* is formed, such as occurs in apes and the edentata. Microscopic retia mirabilia

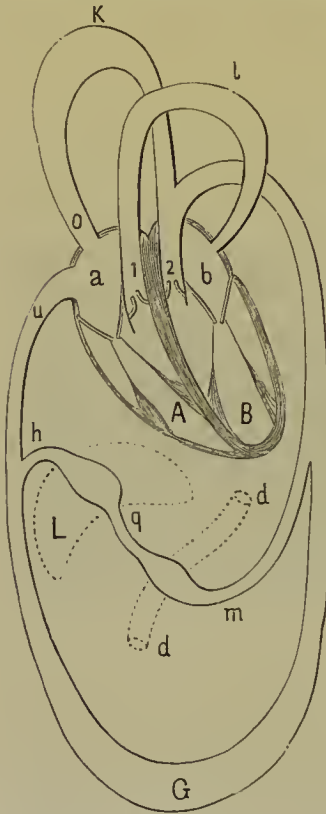


Fig. 33.

Scheme of the circulation.—*a*, right, *b*, left auricle; *A*, right, *B*, left ventricle; *1*, pulmonary artery; *2*, aorta; *l*, area of pulmonary, *K*, area of systemic circulation; *o*, the superior vena cava; *G*, area supplying the inferior vena cava, *u*; *d, d*, intestine; *m*, mesenteric artery; *q*, portal vein; *L*, liver; *h*, hepatic vein.

mirabile is formed, such as

exist in the human mesentery (*Schöbl*). Similar arrangements may exist in connection with veins, giving rise to *venous retia mirabilia*.

43. THE HEART.—The muscular fibres of the mammalian heart consist of short (50 to 70 μ in man), very fine, transversely striated fibres, which are actual unicellular elements, devoid of a sarcolemma (15 to 25 μ broad), and usually divided at their blunt ends, by which means they anastomose and form a network (fig. 34, A, B). The individual muscle-cells contain in their centre an oval nucleus, and are held together by a cement-substance, which is blackened by silver nitrate, and dissolved by a 33 per cent. solution of caustic potash. This cement is also dissolved by a 40 per cent. solution of nitric acid. The transverse striæ are not very distinct, and not unfrequently there is an appearance of longitudinal striation, produced by a number of very small granules arranged in rows within the fibres. The fibres are gathered lengthwise in bundles, or fasciculi, surrounded and separated from each other by delicate processes of the perimysium. When the connective-tissue is dissolved by prolonged boiling, these

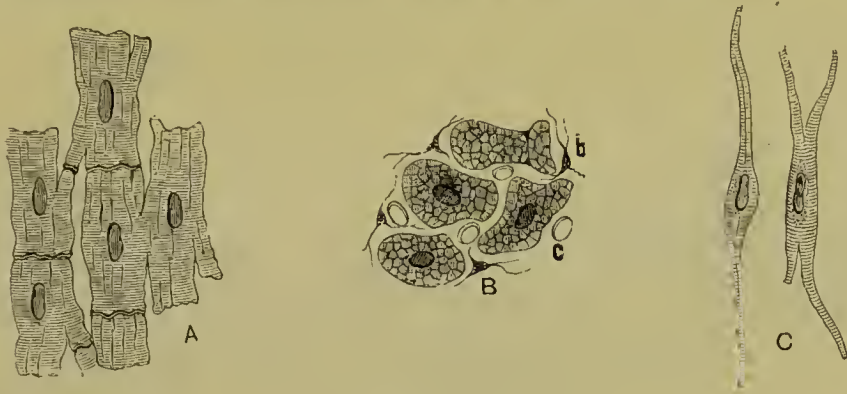


Fig. 34.

A, muscular fibres from the heart of a mammal, and C from a frog; B, transverse section of the cardiac fibres; *b*, connective-tissue corpuscles; *c*, capillaries.

bundles can be isolated, and constitute the so-called "fibres" of the heart. The transverse sections of the bundles in the auricles are polygonal or rounded, while in the ventricles they are somewhat flattened. [The muscular mass of the heart is called the **myocardium**, and is invested by fibrous tissue. It is important to notice that the connective-tissue of the visceral pericardium (**epicardium**) is continuous with that of the endocardium by means of the perimysium surrounding the bundles of muscular fibres.] The fine spaces which exist between these bundles form narrow lacunæ, lined with epithelium, and constituting part of the lymphatic system of the heart.

[The cardiac muscular fibres occupy an intermediate position between striped and plain muscular fibres. Although they are striped, they are involuntary, not being directly under the influence of the will, while they contract more slowly than a voluntary muscle of the skeleton.] In the **frog's heart** the muscular fibres are in shape elongated spindles, or fusiform, in this respect resembling the plain muscle-cells, but they are transversely striped (fig. 34, C). They are easily isolated by means of a 33 per cent. solution of potash or dilute alcohol.

44. ARRANGEMENT OF THE CARDIAC MUSCULAR FIBRES.—The study of the embryonic heart is the key to a proper understanding of the complicated arrangement of the fibres in the adult heart. The simple tubular heart of the embryo has an *outer circular* and an *inner longitudinal* layer of fibres. The septum is formed later; hence, it is clear that a part, at least, of the fibres must be common to the two auricles, and a part also to the two ventricles, since there is, originally, but one chamber in the heart. The muscular fibres of the auricles are, however, *completely separated* from those of the ventricles by the fibro-cartilaginous rings. In the auricles the fundamental arrangement of the embryonic fibres partly remains, while in the ventricles it becomes obscured as the cavities undergo a sac-like dilatation, and also become twisted in a spiral manner.

(1) **The muscular fibres in the auricles** are completely separated from the fibres of the ventricles by the *fibrous* rings which surround the auriculo-ventricular orifices, and which serve as an attachment for the auriculo-ventricular valves (fig. 35, I.).

The auricles are much thinner than the ventricles, and their fibres are generally arranged in two layers; the outer *transverse* layer is continuous over both auricles, whilst the inner one is directed *longitudinally*. The outer transverse fibres may be traced from the openings of the venous trunks anteriorly and posteriorly over the auricular walls. The longitudinal fibres are specially well marked where they are inserted into the fibro-cartilaginous rings, while in some parts of the anterior auricular wall they are not continuous. In the *auricular septum*, some fibres, circularly disposed around the *fossa ovalis* (formerly the embryonic opening of the foramen ovale), are well marked. *Circular bands* of striped muscle exist around the *veins* where they open into the heart; these are least marked on the inferior vena cava, and are stronger and reach higher (2.5 cm.) on the superior vena cava (fig. 35, II.). Similar fibres exist around the pulmonary veins, where they join the left auricle, and these fibres (which are arranged as an inner circular and an outer longitudinal layer) can be traced to the hilus of the lung in man and some

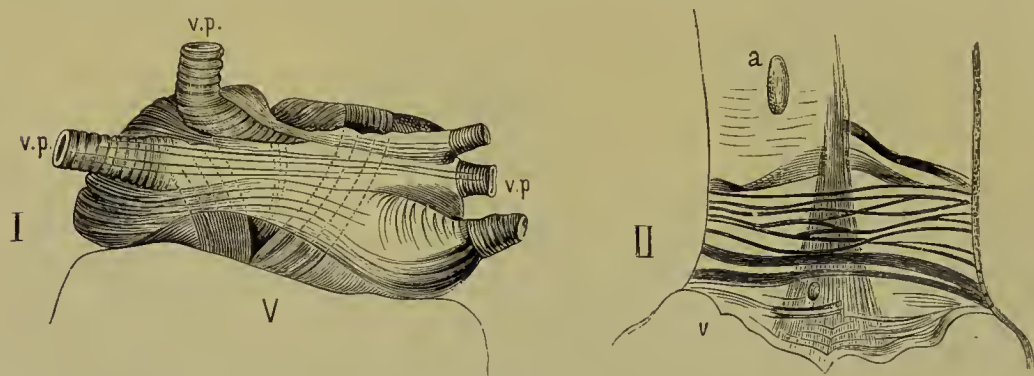


Fig. 35.

- I. Course of the muscular fibres on the left auricle with the outer transverse and inner longitudinal fibres, the circular fibres on the pulmonary veins (*v. p.*); V, the left ventricle (*John Reid*). II. Arrangement of the striped muscular fibres on the superior vena cava (*Elischer*) —a, opening of vena azygos; v, auricle.

mammals; in the ape and rat they extend on the pulmonary veins right into the lung. In the mouse and bat, again, the striped muscular fibres pass so far into the lungs that the walls of the smaller veins are largely composed of striped muscle (*Stieda*).

Circular muscular fibres are found where the vena magna cordis enters the heart, and in the *Valvula Thebesii* which guards it.

Physiological Significance.—(1) The auricles contract *independently* of the ventricles. This is seen when the heart is about to die; when there may be several auricular contractions for one ventricular, and at last only the auricles pulsate. The auricular portion of the right auricle beats longest; hence it is called the “ultimum moriens.” Independent rhythmical contractions of the venæ cavæ and pulmonary veins are often noticed after the heart has ceased to beat. [This beating can also be observed in those veins in a rabbit after the heart is cut out of the body.]

(2) The double arrangement of the fibres (transverse and longitudinal) produces a simultaneous and uniform diminution of the auricular cavity (such as occurs in most of the hollow viscera).

(3) The contraction of the circular muscular fibres around the venous orifices, and the subsequent contraction of the auricle, cause these veins to empty themselves into the auricle; and by their presence and action they prevent any large quantity of blood from passing backward into the veins when the auricle contracts. [No

valves are present in the superior and inferior vena cava in the adult heart, or in the pulmonary veins, hence the contraction of these circular muscular fibres plays an important part in preventing any reflux of blood during the contraction of the auricles.]

45. ARRANGEMENT OF THE VENTRICULAR FIBRES.—(2) The muscular fibres in the thick wall of the ventricles are arranged in several layers under the pericardium (fig. 36, A). First, there is an *outer longitudinal* layer (A), which is in the form of single bundles on the right ventricle, but forms a complete layer on the left ventricle, where it measures about one-eighth of the thickness of the ventricular wall. A *second longitudinal* layer of fibres lies on the *inner surface* of the ventricles, distinctly visible at the orifices, and within the vertically placed papillary muscles, whilst elsewhere it is replaced by the irregularly arranged trabeculæ carneæ. Between these two layers there lies the thickest layer, consisting of *more or less transversely* arranged bundles, which may be broken up into single

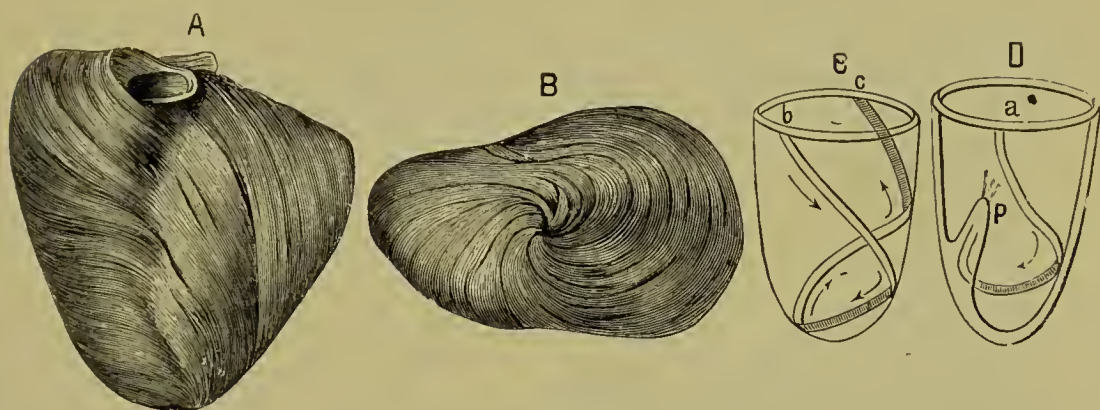


Fig. 36.

Course of the ventricular muscular fibres. A, on the anterior surface; B, view of the apex with the vortex; C, course of the fibres within the ventricular wall; D, fibres passing into a papillary muscle (*p*).

layers more or less circularly disposed. The deep *lymphatic vessels* run between the layers, whilst the *blood-vessels* lie within the substance of the layers, and are surrounded by the primitive bundles of muscular fibres. All three layers are not completely independent of each other; on the contrary, the fibres which run *obliquely* form a gradual *transition* between the transverse layers and the inner and outer longitudinal layers. It is not, however, quite correct to assume that the outer longitudinal layer gradually passes into the transverse, and this again into the inner longitudinal layer (as is shown schematically in C); because, as Henle pointed out, the transverse fibres are relatively far greater in amount. In general, the *outer* longitudinal fibres are so arranged as to cross the *inner* longitudinal layer at an acute angle. The transverse layers lying between these two form gradual transitions between these directions. At the apex of the left ventricle, the outer longitudinal fibres bend or curve so as to meet at the so-called vortex B, where they enter the muscular substance, and, taking an upward and inward direction, reach the papillary muscles, P, D; although it is a mistake to say that all the bundles which ascend to the papillary muscles arise from the vertical fibres of the outer surface; many seem to arise independently within the ventricular wall. According to Henle, all the external longitudinal fibres do not arise from the fibrous rings or the roots of the arteries. The mitral orifice is surrounded by circular fibres which act like a sphincter (*Henle*).

[The assumption that the muscles of the ventricle are arranged so as to form a figure of 8, or in loops, seems to be incorrect; thus, fibres are said to arise at the base of the ventricle, to pass over it, and to reach the vortex, where they pass into the interior of the muscular substance, to end either in the papillary muscles or high up on the inner surface of the heart at its base. Figs. C and D give a schematic representation of this view.]

Only the general arrangement of the ventricular muscular fibres has been indicated. According to Pettigrew, there are seven layers in the ventricle, viz., three external, a fourth or central layer, and three internal. These internal layers are continuous with the corresponding external layers at the apex, thus—one and seven, two and six.

46. PERICARDIUM, ENDOCARDIUM, VALVES.—The pericardium encloses within its two layers [visceral and parietal] a lymph space—the pericardial space—which contains a small quantity of lymph—the **pericardial fluid**. It has the structure of a **SEROUS MEMBRANE**, i.e., it consists of *connective-tissue* mixed with *fine elastic fibres* arranged in the form of a thin delicate membrane, and covered on its free surfaces with a single layer of epithelium or *endothelium*, composed of irregular, polygonal, flat cells. [Like serous cavities generally, it is a closed cavity, and does not communicate with the exterior.] A rich *lymphatic network* lies under the pericardium (fig. 29) and endocardium; also in the deeper layers of the visceral pericardium next the heart and between muscular bundles (*Salvioli*). No stomata exist either on its visceral or parietal layers. Around the coronary arteries of the heart exist lymph-vessels and deposits of fat, which lie in the furrows and grooves in the *subserosa* of the *epicardium* (visceral layer).

The **endocardium**, next the cavity of the heart, consists of a *single* layer of polygonal, flat, nucleated *endothelial* cells. [Under this there is a nearly homogeneous hyaline layer (fig. 37, *a*), slightly thicker on the left side, which gives the endocardium its polished appearance.] Then follows, as the *basis* of the membrane, a layer of *fine elastic fibres*—stronger in the auricles, and in some places thereof assuming the characters of a fenestrated membrane. Between these fibres a small quantity of connective-tissue exists, which is in larger amount and more areolar in its characters next the myocardium. Bundles of *non-striped* muscular fibres (few in the auricles) are scattered and arranged for the most part longitudinally between the elastic fibres. These seem evidently meant to resist the distension which is apt to occur when the heart contracts and great pressure is put upon the endocardium. In all cases where high pressure is put upon walls composed of soft parts, we always find muscular

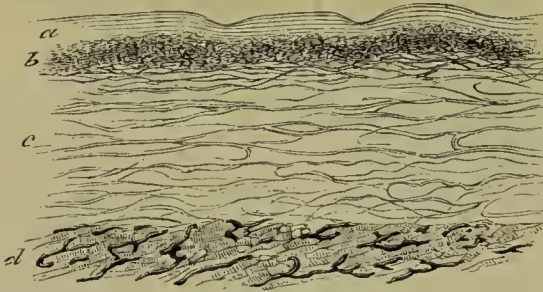


Fig. 37.

Section of the endocardium. *a*, hyaline layer; *b*, network of fine elastic fibres; *c*, network of stronger elastic fibres; *d*, myocardium with blood-vessels, which do not pass into the endocardium.

fibres present, and never elastic fibres alone. No blood-vessels occur in the endocardium (*Langer*).

The **valves** also belong to the endocardium—both the *semi-lunar valves* of the aorta and pulmonary artery, which prevent the blood from passing back into the ventricles, and the *tricuspid* (*right* auriculo-ventricular) and *mitral* (*left* auriculo-ventricular), which protect the auricles from the same result. The lower vertebrata have valves in the orifices of the *venæ cavæ*, which prevent regurgitation into them; while in birds and some mammals these valves exist in a rudimentary condition. The valves are fixed by their base to resistant *fibrous rings*, consisting of elastic and fibrous tissue. They are formed of two layers—(1) the *fibrous*, which is a direct continuation of the fibrous rings, and (2) a layer of *elastic* elements. The elastic layer of the auriculo-ventricular valves is an immediate prolongation of the endocardium of the auricles, and is directed towards the auricles. The semi-lunar valves have a thin elastic layer directed towards the arteries, which is thickest at their base. The connective-tissue layer directed towards the ventricle is about half the thickness of the valve itself.

The **auriculo-ventricular valves** also contain **striped muscular fibres**. Radiating fibres proceed from the auricles and pass into the valves, which, when the

atria contract, retract the valves towards their base, and thus make a larger opening for the passage of the blood into the ventricles; according to Paladino, they raise the valves after they have been pressed down by the blood-current. This observer also described some longitudinal fibres which proceed from the ventricles to enter these valves. There is also a concentric layer of fibres arranged near their point of attachment, and directed more towards their ventricular surface. These fibres seem to contract sphincter-like when the ventricle contracts, and thus approximate the base of the valves, and so prevent too great tension being put upon them. The larger chordæ tendineæ also contain striped muscle, while a delicate muscular network exists in the valvula Thebesii and valvula Eustachii.

Purkinje's Fibres consist of an anastomosing system of greyish fibres which exist in the sub-endocardial tissue of the ventricles, especially in the heart of the sheep and ox. The fibres are made up of polyhedral clear cells, containing some granular protoplasm, and usually two nuclei (fig. 38). The margins of the cells are striated. Transition-forms are found between these cells and the ordinary cardiac fibres; in fact, these cells become continuous with the true fully developed cardiac fibres. They represent cells which have been arrested in their development. They are absent in man and the lower vertebrates, but in birds and some mammals they are well marked (*Schweigger-Seidel, Ranvier*).

Blood-Vessels occur in the auriculo-ventricular valves only where muscular fibres are present, while the semi-lunar valves are usually devoid of vessels except at their base. The best figures of the blood-vessels of the valves are given by Langer and Darier. The network of **lymphatics** in the endocardium reaches towards the middle of the valves.

Weight of the Heart.—According to W. Müller the proportion between the weight of the body and the heart in the child, and until the body reaches 40 kilos., is 5 grms. of heart-substance to 1 kilo. of body-weight; when the body-weight is from 50 to 90 kilos. the ratio is 1 kilo. to 4 grms. of heart-substance; at 100 kilos. 3.5 grms. As age advances, the auricles become stronger. The right ventricle is half the weight of the left. The weight of the heart of an adult man is about 309 grms.; female, 274 grms. [According to Laennec the heart is about the size of the closed fist of the individual.] Blosfeld and Dieberg give 346 grms. for the male, and 310 to 340 grms. for the female heart. The *specific gravity* of the heart-muscle is 1.069. The thickness of the left ventricle in the middle in man is 11.4 mm., and in woman 11.15; that of the right is 4.1 and 3.6 mm. respectively.

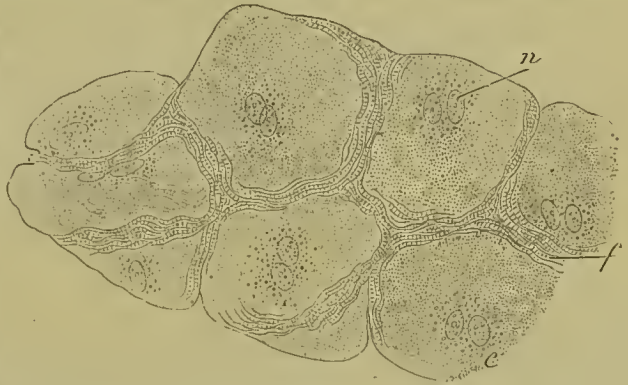


Fig. 38.

Purkinje's fibres isolated with dilute alcohol. *c*, cell; *f*, striated substance; *n*, nucleus. $\times 300$.

47. AUTOMATIC REGULATION OF THE HEART.—**Anatomical Investigations.**—The two coronary arteries arise from the first part of the aorta in the region of the sinus of Valsalva. The position of origin varies—(1) either the orifices lie within the sinus, or (2) their openings are only partially reached by the margins of the semi-lunar valves (which is *usually* the case in the left coronary artery of man and the ox), or (3) their orifices lie clear above the margins of the valves. Post-mortem observations seem to show that during contraction of the ventricle it is very improbable that the semi-lunar valves constantly cover the origin of the coronary arteries.

Automatic Regulation of the Heart.—Brücke attempted to show that during the systole, or contraction of the ventricle, the semi-lunar valves covered the openings of the coronary arteries, so that these vessels could be filled with blood only during the diastole or relaxation of the ventricle. To him it seemed that (a) the diastolic filling of the coronary arteries would help to dilate the ventricles; (b) on the contrary, a systolic filling of these arteries would oppose the contraction, because the systolic filling and expulsion of the blood from the coronary arteries would diminish the force of the ventricular contraction. [To this

supposed arrangement Brücke gave the name "Selbststeuerung," which may be rendered as above, or as "self-controlling" action of the heart by the aortic valves.]

Arguments against Brücke's View.—The following considerations militate against this theory:—(1) Filling the coronary vessels under a high pressure in a dead heart causes a *diminution* of the ventricular cavity (*v. Wittich*). (2) The chief trunks of the coronary arteries lie in loose sub-pericardial fatty tissue in the cardiac sulci, hence a dilatation of the ventricle through this agency is most unlikely (*Landois*). (3) Experiments on animals have shown that a coronary artery spouts, like all arteries, during the systole of the ventricle. Von Ziemssen found that in the case of a woman who had a large part of the anterior wall of the thorax removed by an operation, the heart being covered only by a thin membrane, the pulse in the coronary arteries was synchronous with the pulse in the pulmonary artery. H. N. Martin and Sedgwick placed a manometer in connection with the coronary artery, and another with the carotid in a large dog, and they found that the pulsations occurred *simultaneously*. When a coronary artery is divided, the blood flows out continuously, but undergoes acceleration during the systole of the ventricles (*Endemann, Perls*). (4) If a strong intermittent current of water be allowed to flow through a sufficiently wide tube into the left auricle of a fresh pig's heart, so that the water passes into the aorta, and if the aorta be provided with a vertical tube, the water flows continuously from the coronary arteries, and is accelerated during the systole. (5) It is exceedingly improbable that the coronary arteries should be filled during the diastole, while all the other arteries are filled during systole of the ventricle. (6) There is always a sufficient quantity of blood in the sinus of Valsalva to fill the arteries during the first part of the systole. (7) The valves, when raised, are not applied directly to the aortic wall (*Hamberger, Rüdinger*) even by the most energetic pressure from the ventricle (*Sandborg and Worm Müller*). (8) Observations on voluntary muscles have shown that the small arteries dilate during contraction of the muscle, and the blood-stream is accelerated. (9) By the systolic filling of the aorta the arterial path is elongated—this elastic distension is compensated before the diastole occurs. By the recoil of the aortic walls the layer of blood in them is driven backwards and closes the valves (*Ceradini*). According to Sandborg and Worm Müller, the semilunar valves close just after the ventricles have begun to relax, which agrees with the curve obtained from the cardiac impulse (fig. 39, A).

During the systole, the small arterial trunks lying next the ventricular cavities have to bear a higher pressure than that borne by the aorta, and their lumen must be compressed during the systole so that their contents are propelled towards the veins.

Peculiarities of the Cardiac Blood-Vessels.—The *capillary vessels* of the myocardium are very numerous, corresponding to the energetic activity of the heart. Where they pass into veins, several unite at once to form a wide venous trunk, whereby an easy passage is offered to the blood. The *veins* are provided with valves so that (1) during systole of the right auricle the venous stream is interrupted; (2) during contraction of the ventricles, the blood in the coronary veins is similarly accelerated as in the veins of muscles. The coronary arteries are characterised by their very thick connective-tissue and elastic intima, which perhaps accounts for the frequent occurrence of atheroma of these vessels (*Henle*). Some observers maintain that the coronary arteries do not anastomose, but this is denied by Langer and Krause. [West has injected the one artery from the other.] Many of the small lower vertebrates have no blood-vessels in their heart-muscle, *e.g.*, frog (*Hyrtl*).

Ligature of the Coronary Arteries.—The phenomena produced by partial obliteration or ligature of the coronary arteries are most important. In man analogous conditions occur, as in atheroma or calcification of these arteries. Sée and others have ligatured the coronary arteries in dogs, and found that after two minutes the cardiac contractions gave place to twitchings of the muscular fibres, and ultimately the heart ceased to beat. Ligature of the anterior coronary artery alone, or of both its branches, is sufficient to produce this result. If the coronary arteries be compressed or tied in a rabbit in the angle between the bulbus aortæ and the ventricle, the heart's action is soon weakened, owing to the sudden anæmia and to the retention of the decomposition-products of the metabolism in the heart-muscle. Ligature of one artery first affects the corresponding ventricle, then the other ventricle, and, last of all, the auricles. Hence, compression of the *left* coronary artery (with simultaneous artificial respiration in a curarised animal), causes slowing of the contractions, especially of the left ventricle, whilst the right one at first contracts more quickly, and then gradually its rhythm is slowed. The contractions of the left ventricle are not only slowed but also weakened, whilst

the right pulsates with undiminished force. Hence it follows that, as the left half of the heart cannot expel the blood in sufficient quantity, the left auricle becomes filled, whilst the right ventricle, not being affected, pumps blood into the lungs. Œdema of the lungs is produced by the high pressure in the pulmonary circulation, which is propagated from the right heart through the pulmonary vessels into the left auricle (*Samuelson and Grünhagen*). According to Sig. Mayer, protracted dyspnoea causes the left ventricle to beat more feebly sooner than the right, so that the left side of the heart becomes congested. Perhaps this may explain the occurrence of pulmonary œdema during the death-agony.

Cohnheim and v. Schulthess-Rechberg found, after ligature of one of the large branches of a coronary artery in a dog, that at the end of a minute the pulsations become intermittent. This intermittence becomes more pronounced, the two sides of the heart do not contract simultaneously (*arrhythmia*), the heart beats more slowly, and the blood-pressure falls. Suddenly, about 105 seconds after the ligature is applied, both ventricles cease to beat, and there is a great fall of the blood-pressure. After an arrest lasting for about 10 to 20 seconds, twitching movements occur in the ventricles, while the auricles pulsate regularly, and may continue to do so for many minutes, but the ventricles cease to beat altogether after 50 seconds. According to Lukjanow, there is a peristaltic condition which operates upwards and downwards, and occurs in the period between the regular contraction and the twitching vibratory movement. Stimulation of the vagus does not arrest these peristaltic movements.

Pathological.—In so-called sclerosis of the coronary arteries in old age, there are attacks of diminished cardiac activity, weakness of the heart, and altered rhythm and frequency, with consequent breathlessness; there may also be loss of consciousness, congestions, and attacks of pulmonary œdema. Death may take place unexpectedly from sudden arrest of the heart's action.

48. MOVEMENTS OF THE HEART.—**Cardiac Revolution.**—The movement of the heart is characterised by an alternate contraction and relaxation of its walls.

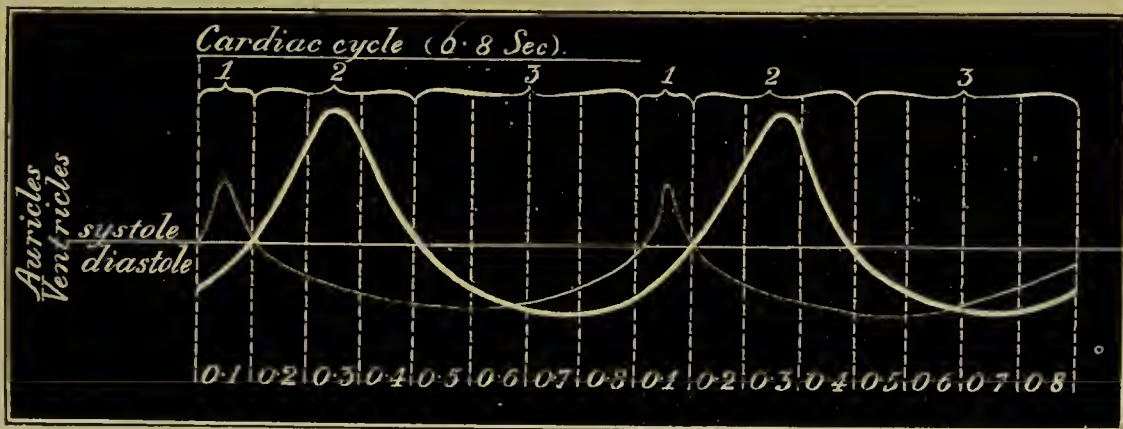


Fig. 39.

Diagram of the sequence of events in the heart during a cardiac cycle.

The total cardiac movement is called a “**cardiac revolution**,” or a “**cardiac cycle**,” and consists of three acts—the contraction or **Systole of the auricles**, the contraction or **Systole of the ventricles**, and the **pause** (fig. 39). During the pause the auricles and ventricles are relaxed; during the contraction of the auricles the ventricles are at rest; whilst during the contraction of the ventricles the auricles are relaxed. The rest during the phase of relaxation is called the **diastole**.

The three events—

Systole of the auricles,
Systole of the ventricles,
Pause,

may be represented by the preceding diagram, while the table shows their relative duration (§ 51).

	LANDOIS.	GIBSON.
Duration of the auricular systole,	0·170 – 0·177	0·100 – 0·130
Do. ventricular systole,	0·309 – 0·346	0·325 – 0·395
Do. pause,	0·393 – 0·407	0·455 – 0·690

The following is the **sequence of events in the heart during a cardiac cycle** :—
(A) The blood flows into the auricles, and thus distends them and the auricular appendices. This is caused by—

(1) The *pressure* of the blood in the venæ cavae (right side) and the pulmonary veins (left side) being greater than the pressure in the auricles. (2) The *elastic*

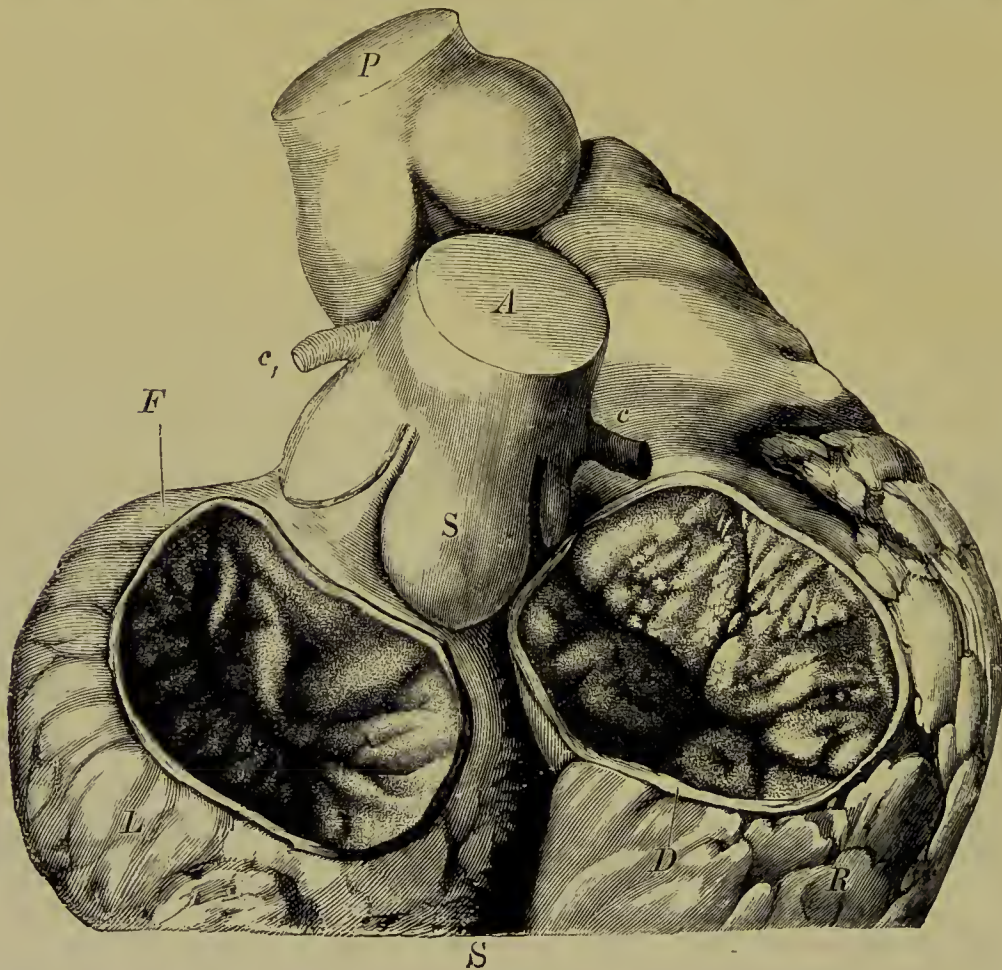


Fig. 40.

Cast of the ventricles of the human heart viewed from *behind* and above; the walls have been removed, and only the fibrous rings and the auriculo-ventricular valves are retained. *L*, left, *R*, right ventricle; *S*, septum; *F*, left fibrous ring, with mitral valve closed; *D*, right fibrous ring, with tricuspid closed; *A*, aorta, with the left (*C*₁) and right (*C*) coronary arteries; *S*, sinus of Valsalva; *P*, pulmonary artery.

traction of the lungs (§ 68), which, after complete systole of the auricles, pulls asunder the now relaxed and yielding auricular walls. The auricular appendages are also filled at the same time, and they act to a certain extent as accessory reservoirs for the large supply of blood streaming into the auricles.

(B) The auricles contract, and we observe in rapid succession—

(1) The contraction and emptying of the auricular appendix towards the atrium. Simultaneously the mouths of the veins become narrowed, owing to the contraction

of their circular muscular fibres (more especially the superior vena cava and the pulmonary veins); (2) the auricular walls contract simultaneously towards the auriculo-ventricular valves and the venous orifices, whereby (3) the blood is driven into the relaxed ventricles, which are considerably distended thereby.

The contraction of the auricles is followed by—

(a) A slight stagnation of the blood in the large venous trunks, as can be observed in a rabbit after division of the pectoral muscles so as to expose the junction of the jugular with the subclavian vein. There is no actual regurgitation of the blood, but only a partial interruption of the inflow into the auricles, because the mouths of the veins are contracted, and the pressure in the superior vena cava and pulmonary veins soon holds in equilibrium any reflux of blood; and lastly, because any reflux into the cardiac veins is prevented by valves. The movement of the heart causes a regular pulsatile phenomenon in the blood of the *venæ cavæ*, which under abnormal circumstances may produce a venous pulse (see § 99).

(b) The chief motor effect of the contraction of the auricles is the *dilatation of the relaxed ventricle*, which has already been dilated to a slight extent by the *elastic traction* of the lungs.

Aspiration of the Ventricles.—The dilatation of the ventricles has been ascribed to the elasticity of the muscular walls—the strongly contracted ventricular walls (like a compressed india-rubber bag), in virtue of their elasticity, are supposed, in returning to their normal resting form, to suck in or aspirate the blood under a negative pressure; this power on the part of the ventricle is not great (p. 68).

(c) When the ventricles are distended by the inflowing blood, the auriculo-ventricular valves are floated up, partly by the recoil or reflexion of the blood from the ventricular wall, and partly owing to their lighter specific gravity, whereby they easily float into a more or less horizontal position. The valves are also raised to a slight extent by the longitudinal muscular fibres, which pass from the auricles into the cusps of the valve.

(C) The ventricles now contract, and simultaneously the auricles relax, whereby—

(1) The muscular walls contract forcibly from all sides, and thus diminish the ventricular cavity. (2) The blood is at once pressed against the under surface of the auriculo-ventricular valves, whose curved margins are opposed to each other like teeth, and are pressed hermetically against each other (fig. 40). It is impossible for the blood to push the cusps backwards into the auricle, as the *chordæ tendineæ* hold fast their margins and surfaces like a taut sail. The margins of the neighbouring cusps are also kept in apposition, as the *chordæ tendineæ* from one papillary muscle always pass to the adjoining edges of two cusps. The extent to which the ventricular wall is shortened is compensated by the contraction of the papillary muscle, and also of the large muscular *chordæ*, so that the cusps cannot be pushed into the auricle. When the valves are closed, their surfaces are horizontal, so that, even when the ventricles are contracted to their greatest extent, there remains in the *supra-papillary space* a small amount of blood which is not expelled (*Sandborg and Worm Müller*). (3) When the pressure within the ventricles exceeds that in the arteries, the semi-lunar valves are forced open and stretched like a sail across the pocket-like sinus, without, however, being directly applied to the wall of the arteries (pulmonary and aorta), and thus the blood enters the arteries.



Fig. 41.

The closed semi-lunar valve of the pulmonary artery seen from below.

(D) Pause.—As soon as the ventricular contraction ends, and the ventricles begin to relax, the *semi-lunar valves close* (fig. 41). The diastole of the ventricles

is followed by the **pause**. Under normal circumstances, the right and left halves of the heart always contract or relax uniformly and simultaneously.

Endocardial Pressure and Negative Pressure in the Ventricle.—Goltz and Gaule found that there was a *negative pressure* of 23·5 mm. Hg. (dog) in the interior of the ventricle during a certain phase of the heart's action. This they determined by a maximal and minimal manometer. They surmised that this phase coincided with the *diastolic dilatation*, for which they assumed a considerable power of aspiration. Moens is of opinion that this negative pressure within the ventricle obtains *shortly before the systole has reached its height, i.e.*, just before the inner surface of the ventricles and the valves, after the blood is expelled, are nearly in apposition. He explains this aspiration as being due to the formation of an empty space in the ventricle caused by the energetic expulsion of the blood through the aorta and pulmonary artery.

[**Maximum and Minimum Manometer.**—Into the tube connecting the interior of the ventricle of the heart with the ordinary U-shaped mercury manometer, is introduced the maximum manometer, which is constructed on the principle of a ball and cup valve (fig. 42), the ball A, being kept closed in B by a spring C. To make it a maximum manometer the end A is con-

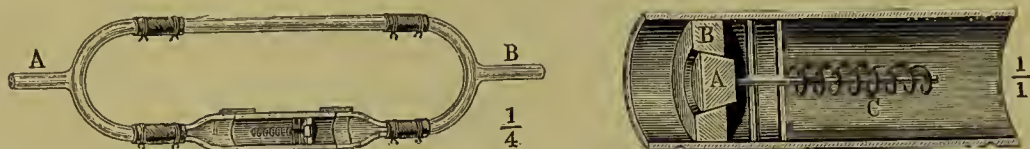


Fig. 42.

Gaule's maximum and minimum manometer A B. $\frac{1}{4}$ shows the actual size and arrangement of the valve.

connected with the heart, and B with the mercurial manometer (fig. 42). When a clamp is placed on the upper limb the valve is acted on only at each systole of the heart, blood is driven beyond it, but during diastole it closes and no blood can return. This goes on until the pressure beyond the valve in the mercury manometer is the same as in the heart. If the valve be reversed, it is converted into a minimum manometer.]

49. PATHOLOGICAL CARDIAC ACTION.—**Cardiac Hypertrophy.**—All resistances to the movement of the blood through the various chambers of the heart, and through the vessels communicating with it, cause a greater amount of work to be thrown upon the portion of the heart specially related to this part of the circulatory system; consequently, there is produced an increase in the thickness of the muscular walls and dilatation of the heart. If the resistance or obstacle does not act upon *one* part of the heart alone, but on parts lying in the *onward* direction of the blood-stream, these parts also subsequently undergo hypertrophy. If in addition to the muscular thickening of a part of the heart, the cavity is simultaneously dilated, it is spoken of as **eccentric hypertrophy** or **hypertrophy with dilatation**. The obstacles most likely to occur in the *blood-vessels* are narrowing of the lumen or want of elasticity in their walls; in the *heart*, narrowing of the arterial or venous orifices or insufficiency or incompetency of the valves. Incompetency of the valves forms an obstruction to the movement of the blood, by allowing part of the blood to flow back or regurgitate, thus throwing extra work upon the heart.

Thus arise—(1) **Hypertrophy of the left ventricle**, owing to resistance in the area of the systemic circulation, especially in the arteries and capillaries—not in the veins. Amongst the causes are—constriction of the orifice or other parts of the aorta, calcification, atheroma, and want of elasticity of the large arteries and irregular dilatations or aneurisms in their course; insufficiency of the aortic valves, in which case the same pressure always obtains within the ventricle and in the aorta; and, lastly, cirrhosis of the kidneys, whereby the excretion of water by these organs is diminished. Even in mitral insufficiency, compensatory hypertrophy of the left ventricle must occur, owing to the hypertrophy of the left atrium in consequence of the increased blood-pressure in the pulmonary circuit.

(2) **Hypertrophy of the left auricle** occurs in stenosis or constriction of the left auriculo-ventricular orifice, or in insufficiency of the mitral valve, and it occurs also as a result of aortic insufficiency, because the auricle has to overcome the continual aortic pressure within the ventricle.

(3) **Hypertrophy of the right ventricle** occurs (*a*) when there is resistance to the blood-stream through the pulmonary circuit. The resistance may be due to (*a*) obliteration of large vascular areas in consequence of destruction, shrinking or compression of the lungs, and the disappearance of numerous capillaries in emphysematous lungs; (*b*) overfilling of the pulmonary circuit with blood in consequence of stenosis of the left auriculo-ventricular orifice, or mitral insufficiency—consequent upon hypertrophy of the left auricle resulting from aortic

insufficiency. (b) When the valves of the pulmonary artery are insufficient, thus permitting the blood to flow back into the ventricle, so that the pressure within the pulmonary artery prevails within the right ventricle (very rare).

(4) **Hypertrophy of the right auricle** occurs in consequence of the last-named condition, and also from stenosis of the tricuspid orifice, or insufficiency of the tricuspid valve (rare).

Artificial Injury to the Valves.—If the aortic valves are perforated, with or without simultaneous injury to the mitral or tricuspid valves, the heart does more work; thus the physical defect is overcome for a time, so that the blood-pressure does not fall. The heart seems to have a store of reserve energy which is called into play. Soon, however, dilatation takes place, on account of the regurgitation of the blood into the heart. Hypertrophy then occurs, but the compensation meanwhile must be obtained through the reserve energy of the heart (*O. Rosenbach*).

Impeded Diastole.—Among causes which hinder the diastole of the heart are—copious effusion into the pericardium, or the pressure of tumours upon the heart. The systole is greatly interfered with when the heart is united to the pericardium and to the connective tissue in the mediastinum. As a consequence, the connective tissue, and even the thoracic wall, are drawn in during contraction of the heart, so that there is a retraction of the region of the apex-beat during systole, and a protrusion of this part during the diastole.

Palpitation is a symptom indicating generally very rapid and quick action of the heart, the pulsations often being unequal in time and intensity, while the person is generally conscious of the irregularity of the cardiac action. It may be due to some *organic* condition of the heart itself, especially where the cardiac muscles are weak, in cases of dilatation and hypertrophy of the left ventricle, where the heart is gradually becoming unable to overcome the resistances offered to its work, and especially during exertion when the heart is taxed above its strength. It may also occur where the blood-pressure is low, as in anæmia, so that the heart contracts quickly, there being little resistance opposed to its action. The excitability of the cardiac muscle may be increased as in fatty heart, when very slight exertion may excite it often in a paroxysmal way. In other cases, it is *nervous* in its origin, being either direct or reflex. In very emotional and excitable people (especially in women) it is easily set up, and in some people it may be produced reflexly by gastric or intestinal irritation or dyspepsia. It also frequently results from excesses of all kinds and the over-use of tobacco. The remedies to be used obviously depend on the cause. Where the blood-pressure is low, as in anæmia, digitalis and iron will do good; the former by increasing the blood-pressure, and the latter by improving the general nutrition of the body and the blood in particular. In neurotic cases cardiac sedatives are indicated, while in cases due to indigestion hydrocyanic acid is useful (*Branton*).]

Fainting or Syncope.—In fainting the person loses consciousness, owing to a sudden arrest of the blood-supply to the brain, the face is pallid, the respiration is feeble or ceases, while the heart beats but feebly or not at all. The defective supply of blood to the brain may depend upon sudden arrest of the heart's action, caused, it may be, by a fright, or the heart's action may be arrested reflexly. Any cause which suddenly diminishes the blood-pressure may produce it, or when pressure is suddenly removed from the large vessels, as in tapping the abdomen in ascites, without at the same time giving sufficient support to the abdominal viscera. When a person has been long in the recumbent position, on being rapidly set up in bed he may faint. In some forms of heart disease, sudden exertion or change of posture may produce it.]

Treatment.—The object is to restore consciousness and the action of the heart. Place the person in the horizontal position, keep the head low, even lower than the body, and do not support it with pillows. Dashing cold water on the face, so as to stimulate the fifth nerve, usually succeeds in causing the person to take a deep inspiration. In other cases a snuff of smelling salts or ammonia, acting through the nasal branch of the fifth nerve, will excite the cardiac and respiratory functions (§ 368).]

50. THE APEX-BEAT CARADIOGRAM.—**Cardiac Impulse.**—By the term “apex-beat” or “cardiac impulse,” or “precordial pulsation” is understood under normal circumstances an elevation (perceptible to touch and sight), in a circumscribed area of the *fifth left* intercostal space, and caused by the movement of the heart. [The term “precordial” is applied to the part of the chest situated in front of the heart. The cardiac impulse is felt, and is normally visible in the fifth left intercostal space, 2 inches below the nipple, and $\frac{1}{2}$ to 1 inch to its sternal side, or at a point 2 inches to the left of the sternum, *i.e.*, about 3 inches from mid-sternum.] The impulse is more rarely felt in the fourth intercostal space, and it is much less distinct when the heart beats against the fifth rib itself. The position and force of the cardiac impulse vary with changes in the position of the body. [The term “apex-beat” is very loosely applied, but normally it is produced by the impulse of the apex of the left ventricle against the thoracic wall.]

[The cardiac impulse is synchronous with the systole of the heart, but although this name and apex-beat are frequently used as synonymous terms, it is to be remembered that the impulse may be caused by different parts of the heart being in contact with the chest-wall. The cardiac impulse is usually higher than normal in children, while it is lower during inspiration than expiration.]

[Methods.—To obtain a curve of the apex-beat or a **cardiogram**, we may use one or other of the following **cardiographs** (fig. 43). Fig. 43, *A*, is the first form used by Marey, and it consists, of an oval wooden capsule applied in an air-tight manner over the apex-beat. The disc, *p*, capable of being regulated by the screw, *s*, presses upon the region of the apex-beat, while *t* is a tube which may be connected with a recording tambour (fig. 55). *B* is an improved form of the instrument, consisting essentially of a tambour, while attached to the membrane is a button,

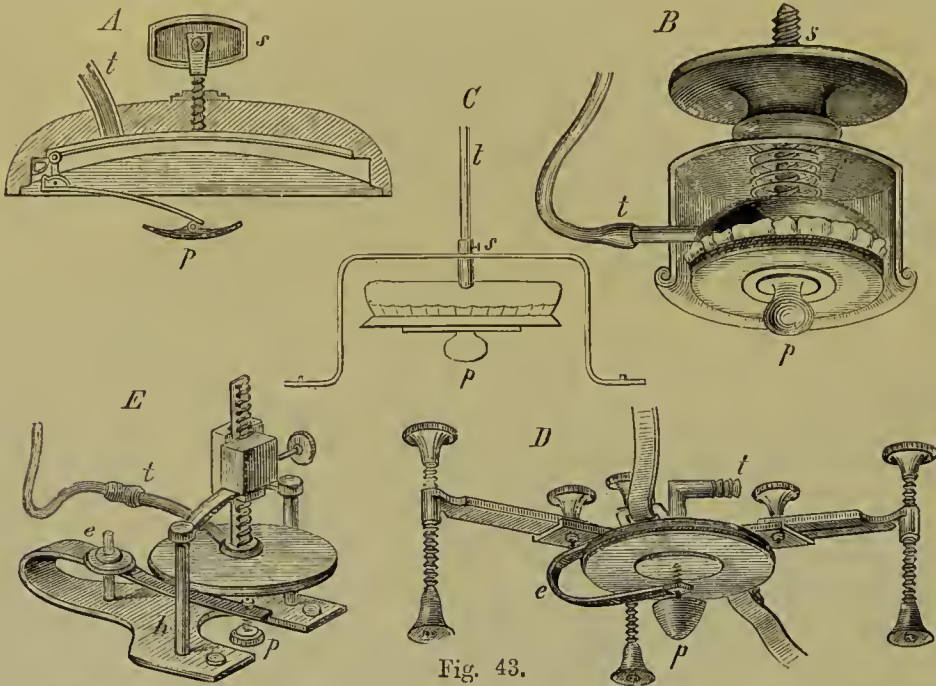


Fig. 43.

Cardiographs. *A*, Marey's original form; *B*, Marey's improved form; *C*, pansphygmograph of Brondgeest; *D*, cardiograph of Burdon-Sanderson; *E*, that of v. Knoll.

p, to be applied over the apex-beat. The movements of the air within the capsule are communicated by the tube, *t*, to a recording tambour. Fig. 43, *C*, is the pansphygmograph of Brondgeest, which consists of a Marey's tambour, in an iron horse-shoe frame, and adjustable by means of a screw, *s*. Burdon-Sanderson's cardiograph is shown in *D*. The button, *p*, carried by the spring, *e*, does not rest upon the caoutchouc membrane, but on an aluminium plate attached to it. The apparatus is adjusted to the chest by three supports. Fig. 43, *E*, shows a modified instrument on the same principle by Grummach and v. Knoll. In all these figures the *t* indicates the exit-tube communicating with a recording tambour (fig. 55). *D* and *E* may be used for other purposes, *e.g.*, for the pulse, so that they are **polygraphs**. See also fig. 88.]

[For studying the curve of contraction and expansion of the ventricles Roy and Adami used a special **myo-cardiograph**. Fine hooks were inserted into the ventricular wall, the hooks were attached to threads which hooked over pulleys and were then connected with recording levers. To obtain tracings of the contraction of the **papillary muscles** a fine hooked wire was inserted through the auricular wall and hooked over one of the mitral flaps. It slides easily in a collar which is tied to the edges of the opening in the auricular wall. To the wire is attached a thread, which, after passing round a pulley, is attached to a recording lever.]

Fig 47, *A*, shows the **cardiogram** or the impulse-curve of the heart of a healthy man; *B*, that of a dog, obtained by means of a sphygmograph. In both, the following points are to be noticed:—*ab*, corresponds to the time of the pause and the contraction of the auricles. As the atria contract in the direction of the axis of the heart from the right and above towards the left and below, the apex of the heart moves towards the intercostal space. The two or three smaller elevations are

perhaps caused by the contractions of the ends of the veins, the auricular appendices, and the atria themselves.

The portion *bc*, which communicates the greatest impulse to the instrument, and also to one's hand when it is placed on the apex-beat, is caused by *the contraction of the ventricles*, and during it the first sound of the heart occurs. By some observers the cardiac impulse has been ascribed to the contraction of the ventricles alone. It, however, is due to all those conditions which cause an elevation in the region of the cardiac impulse.

[Edgren recorded a human cardiogram, and listened at the same time to the heart-sounds, recording the latter by means of an electric signal. The curve rises at *a*, with the beginning of the first sound, *i.e.*, with the contraction of the ventricles, and reaches the abscissa at *f* with the beginning of the second sound, *i.e.*, when the semi-lunar valves are closed. The relation between *a* and the points intermediate between it and *f*, and to the pulse-curve of the carotid, is shown in fig. 45. The letters with the dash correspond to the unmarked letters in the cardiogram.]

[While all observers are agreed as to the position of the occurrence of the first sound in a cardiogram, they differ very considerably as to the position of the second sound, *i.e.*, the closure of the semi-lunar valves (fig. 46). Martius places it in the depression between *e* and *d* (fig. 47, E); Landois at the two projections *d* and *e*, *d* corresponding to the closure of the aortic, and *e* to that of the pulmonary valves; Marey and Fredericq about the middle between *e* and *f*, and Edgren at the point *f*. According to Landois, the part *bc* (fig. 47, A) is due to the contraction of the ventricles, and from *e* onwards the ventricular musculature begins to relax and lasts from *e* to *f*. It is plain from the diagram that according to Landois the closure of the semi-lunar valves takes place earlier (at *d* and *e*) than according to Marey is the case. Fredericq has recently re-investigated the subject on the dog's heart, and agrees with Marey that the closure of the semi-lunar valves takes place at *e*. See also fig. 46.]

The **cause of the cardiac impulse** has been much discussed. It depends upon the following:—

(1) The base of the heart (auriculo-ventricular groove) represents during diastole a *transversely-placed ellipse* (fig. 48, I., FG), while during contraction it has a more *circular figure*, *ab*. Thus, the long diameter of the ellipse (FG) is diminished, the small diameter *dc* is increased, while the base is brought nearer to the chest-wall *e*. This alone does not cause the impulse, but the basis of the heart, being hardened during the systole and brought nearer to the chest-wall, allows the apex to execute the movement which causes the impulse (p. 69).

(2) During relaxation the ventricle lies with its apex (fig. 48, II., *i*) obliquely downwards, and with its long axis in an oblique direction—so that the angles (*bei*, *aci*) formed by the axis of the ventricles with the diameter of the base are unequal—during systole it represents a regular cone, with its axis at right angles to its base. Hence the apex (*i*) must be erected from below and behind (*p*), forwards



Fig. 44.

Cardiogram. *a-f*; 1, beginning of 1st, and 2, 2nd sound.

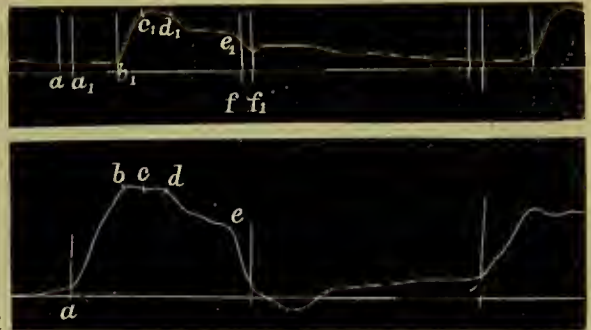


Fig. 45.

The upper curve from the human carotid; the lower a cardiogram taken simultaneously.

and upwards (*Harvey*—"cor sese erigere"), and when hardened during systole presses itself into the intercostal space (fig. 48, II.).

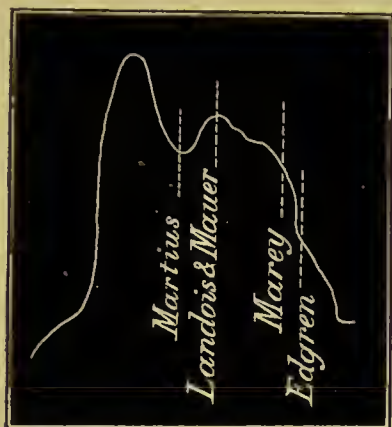


Fig. 46.

Cardiogram of dog, showing the various points of a cardiogram to which different observers have referred the occurrence of the second sound (closure of the semi-lunar valves).

(3) The ventricles undergo during systole a slight spiral twisting on their long axis ("lateralem inclinationem"—*Harvey*), so that the apex is brought from behind more forward, and thus a greater portion of the left ventricle is turned to the front. This rotation is caused by the muscular fibres of the ventricles, which proceed from that part of the fibrous rings between the auricles and ventricles which lies next the anterior thoracic wall. The fibres pass from above obliquely downwards, and to the left, and also run in part upon the posterior surface of the ventricles. When they contract in the axis of their direction, they tend to raise the apex, and also to bring more of the posterior surface of the heart in relation with the anterior thoracic wall. It is favoured by the slightly spiral arrangement of the aorta and pulmonary artery.

These are the most important causes, but the minor causes are—

(4) The "reaction impulse" or "recoil," or that movement which the ventricles

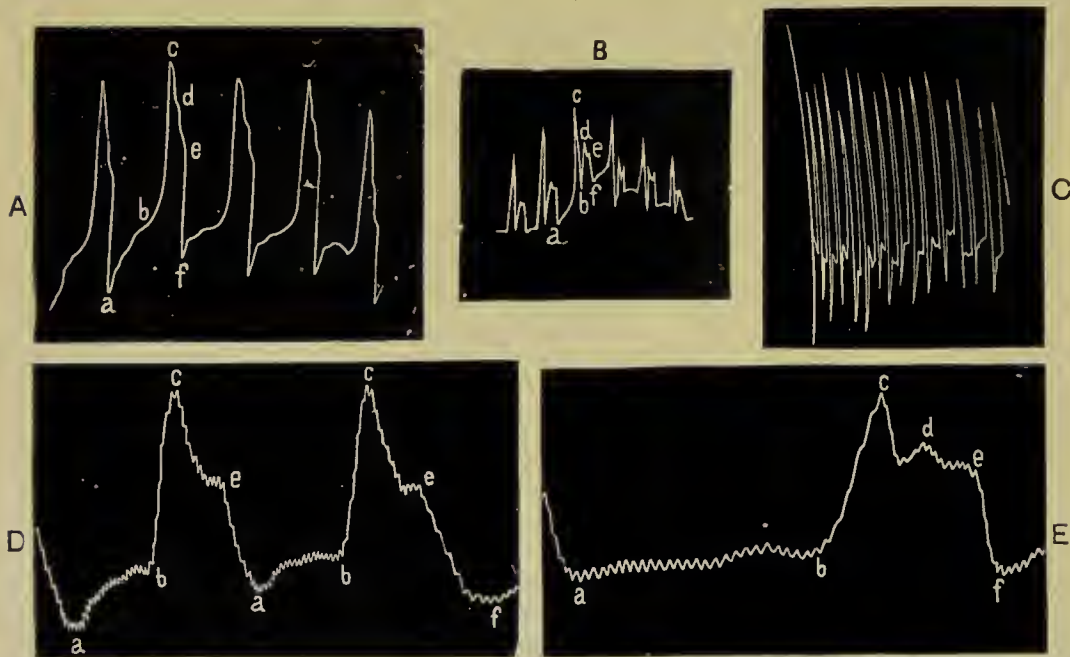


Fig. 47.

Curves from the apex-beat. A, normal curve (man); B, from a dog, C, very rapid curve (dog); D and E, normal curves (man) registered on a vibrating glass plate where each indentation = 0.01613 sec. In all the curves *ab* means contraction of the auricles, and *bc* of the ventricles; *d*, closure of the aortic, and *e*, of the pulmonary valves; *f*, diastole of the ventricle.

are said to undergo (like an exploded gun or rocket) at the moment when the blood is discharged into the aorta and pulmonary artery, whereby the apex goes in

the opposite direction, *i.e.*, downwards and slightly outwards. Landois, however, has shown that the mass of blood is discharged into the vessels 0·08 of a second after the beginning of a systole, while the cardiac impulse occurs with the first sound.

(5) When the blood is discharged into the aorta and pulmonary artery, these vessels are slightly *elongated*, owing to the increased blood-pressure. As the heart is suspended from above by these vessels, the apex is pressed slightly downwards and forwards towards the intercostal space (?).

As the cardiac impulse is observed in the empty hearts of dead animals, (4) and (5) are certainly of only second-rate importance. Filehne and Pentzoldt maintain that the apex during systole does not move to the left and downwards, as must be the case in (4) and (5), but that it moves upward and to the right—a result corroborated by v. Ziemssen. [Barr attributes the cause of the impulse to the rigidity or hardening of the ventricle during systole to the rotatory movement

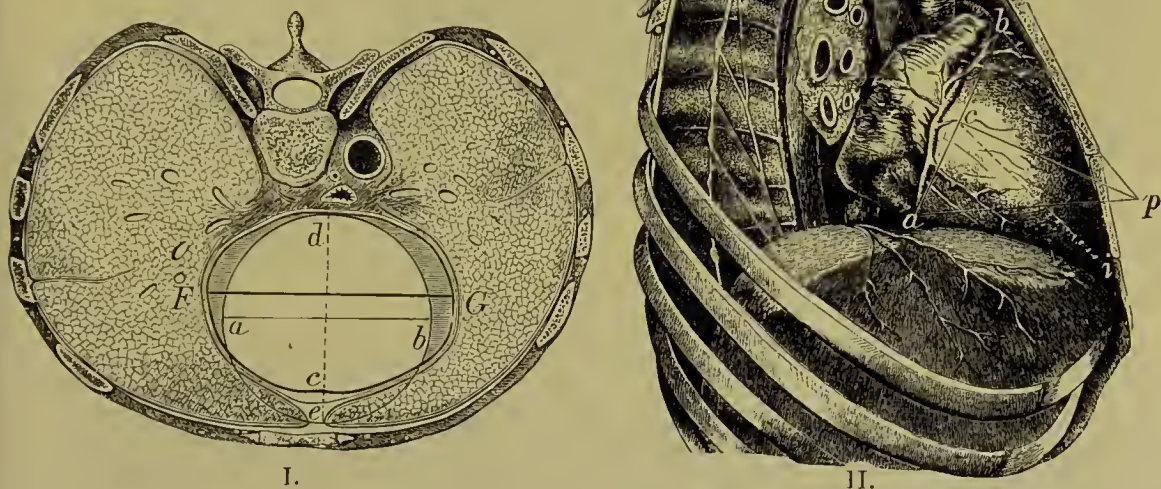


Fig. 48.

- I. Schematic horizontal section through the heart, lungs, and thorax, to show the change of shape which the base of the heart undergoes during contraction of the ventricle—F, G, transverse diameter of the ventricle during diastole; c, position of the thoracic wall; a, b, transverse diameter of the heart during systole, with e, position of the anterior thoracic wall during systole. II. Side-view of the heart—i, apex during diastole; p, during systole.

and lengthening downwards of the blood column in the aorta and pulmonary artery, while towards the end of the systole the maximum of recoil takes place and also contributes to cause it.]

It is to be remembered that as the apex is *always* applied to the chest-wall, separated from it merely by the thin margin of the lung, it only presses against the intercostal space during systole (*Kiwisch*).

After the apex of the curve, c, has been reached at the end of the systole, the curve falls rapidly, as the ventricles quickly become relaxed. In the descending part of the curve, at d and e, are two elevations, which occur *simultaneously with the second sound*. These are caused by the sudden closure of the semi-lunar valves, whereby an impulse is propagated through the axis of the ventricle to its apex, and thus causes a vibration of the intercostal space; d corresponds to the closure of the aortic valves, and e to the closure of the pulmonary valves. The closure of the valves in these two vessels is not simultaneous, but is separated by

an interval of 0.05 to 0.09 sec. The aortic valves close sooner on account of the greater blood-pressure there. Complete diastolic relaxation of the ventricle occurs from *e* to *f* in the curve.

It is clear, then, that the cardiac impulse is caused chiefly by the contraction of the ventricles, while the auricular systole and the vibration caused by the closure of the semi-lunar valves are also concerned in its production.

[Fig. 49 (1) shows a cardiogram obtained from a case of ectopia cordis, and side by side with it is (2) a tracing from the heart of a cat, which was obtained by resting

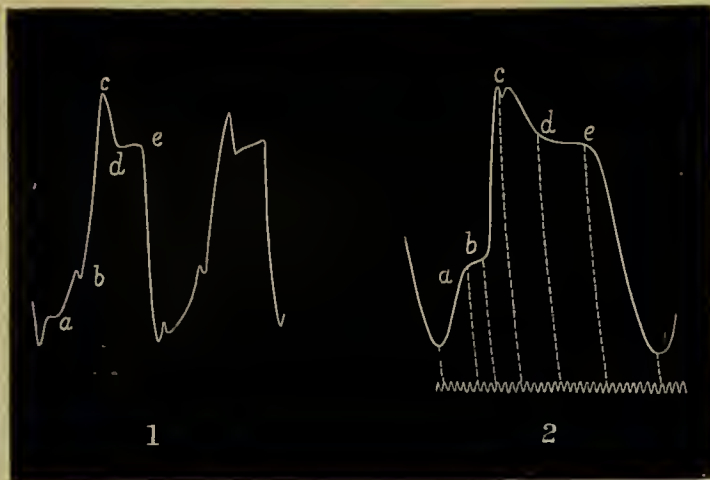


Fig. 49.

1. Cardiographic tracing from a case of ectopia cordis (*François Franck*). 2. Cardiographic tracing from the exposed heart of a cat, obtained by placing a light lever on the ventricle. The tuning-fork curve marks 50 vibrations per sec.

a light lever on the anterior wall of the left ventricle, the organ being exposed by making a hole in the thorax. The two curves are identical in character. In each a rounded wave (*a* to *b*) is followed by a rapid ascent of the curve (*b* to *c*), while the summit or plateau shows a notch (*d*), and a more or less rounded shoulder (*e*) preceding the descent. The part of the curve between *b* and *e* corresponds to the contraction of the ventricle, and from *e* onwards to its relaxation.]

[Some light is thrown on the cardiogram if simultaneously with the taking of a cardiographic tracing the intra-ventricular pressure be measured. Rolleston's method (p. 75), fig. 50 (A) shows such a tracing. A shows the changes in the antero-posterior diameter of the ventricles, but it is to be noted that the highest point of A does not correspond with the maximum pressure within the ventricle, but that the latter occurs at the same time as the notch (4) of A. The notch (4) in A corresponds in time with the interposed wave (4) of B. The descent in A from 3-4 is due to the ventricles having reached their maximum of contraction, and forcing out some blood into the aorta and pulmonary artery, so that their antero-posterior diameter necessarily diminishes. What is the cause of the notch at the moment of maximum intra-ventricular pressure? It corresponds in time with the rapid contraction of the papillary muscles, which thus pull down the auriculo-ventricular valves, thus raising the intra-ventricular pressure; but at the same time the part of the ventricular wall from which the papillary muscles originate becomes indented (*Roy and Adami*).]

[Change in Shape of Heart.]—The experiments of Ludwig and Hesse on the heart of the dog show that the shape of the ventricles varies remarkably in systole and diastole, and that the shape of the heart as found post-mortem is not its natural shape. Broadly speaking, the ventricles during systole become tense and resisting and they are smaller than during diastole, the difference being equal to the amount of blood expelled at systole. As regards form, they change from a somewhat hemispherical figure with an irregular elliptical base, and assume a more regular cone-like form with a circular base, so that the transverse diameter is diminished, the antero-posterior diameter increased.]

[**Method.**—Bleed a dog rapidly from the carotids, defibrinate the blood, expose the heart, tie graduated straight tubes into the pulmonary artery and aorta, and ligature the auricular vessels. Pour the blood into the heart until it is dilated under a pressure equal to the mean arterial pressure (150 mm.). The ventricles are in the diastolic phase, the auricles still pulsate. A plaster cast is now rapidly made of the ventricles. This represents the diastolic phase. To obtain what may be regarded as the systolic phase, a heart, similarly prepared but emptied of blood, is suddenly plunged into a hot (50° C.) saturated solution of potassic bichromate, when the heart gives one rapid and final contraction and remains permanently contracted owing to the heat-rigor, its proteids being coagulated (§ 295). This is the systolic phase. Little pins with twisted points are previously inserted in the organ to mark certain parts of both hearts for comparison.]

[In **diastole**, the shape of the ventricle is hemispheroidal, the apex being rounded, while the posterior surface is flatter than the anterior (fig. 51, A). In the plane of the ventricular base, the greatest diameter is from right to left, and the shortest from base to apex. The conus arteriosus is above the plane of the base. During **systole** the apex is more pointed, the ventricle more conical, while all the diameters in the plane of the base are equally diminished, hence the vertical measurement from base to apex is longer now than either of the diameters at the base (fig. 51, C). The conus arteriosus sinks towards the plane of the base, while the base of the ventricle becomes more circular, so that the difference of the curvatures of the anterior and posterior surfaces vanishes (fig. 51, B). In all these figures the shaded part represents diastole and the clear part systole. The most remarkable point is that the vertical measurement remains unchanged. This refers to the left ventricle, which of course forms the apex; the right is shortened. The plane of the ventricular base in systole is about one-half of what it is in diastole, as is shown in fig. 52.

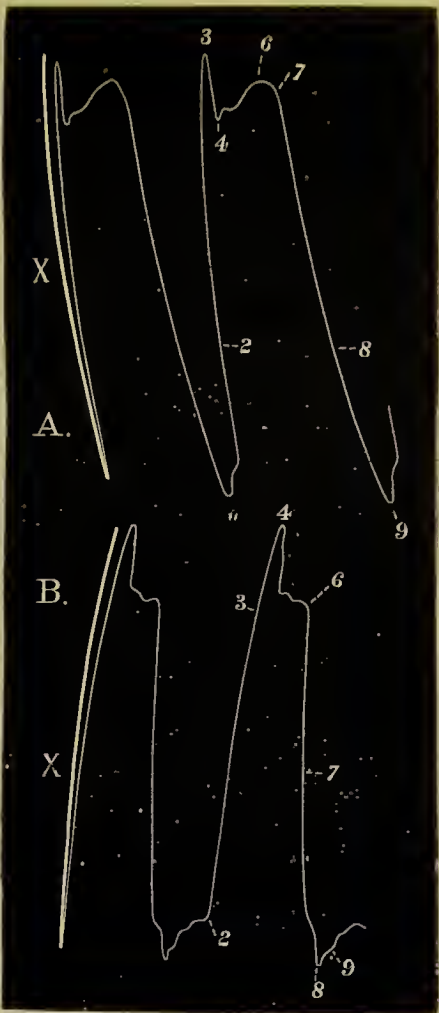


Fig. 50.
A, Cardiogram of the apex-beat (dog);
B, intra-ventricular pressure taken simultaneously. The corresponding parts of the two curves are indicated by letters. ₄

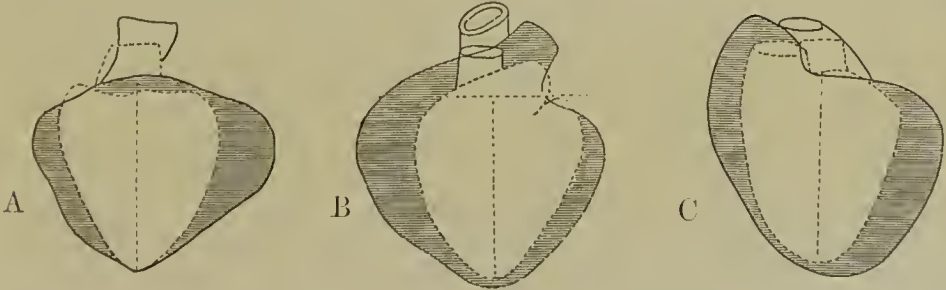


Fig. 51.

A, Projection of a dog's heart—posterior surface; B, anterior surface; C, left lateral surface. Thus the heart is diminished in all its diameters except one, the arterial orifices are scarcely affected, while the area of the auriculo-ventricular orifices (M, T) is dimi-

nished about one-half (fig. 53). This is most important in connection with the closure of the auriculo-ventricular valves; as it shows that the muscular fibres of the heart, by diminishing these orifices during systole, greatly aid in the perfect closure of these valves. Thus we explain why defective nutrition of the cardiac muscle may

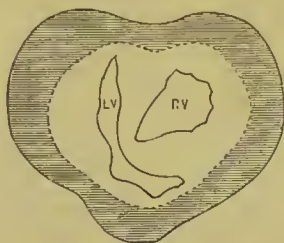


Fig. 52.

Projection of the base in systole and diastole; RV, right, and LV, left ventricle.

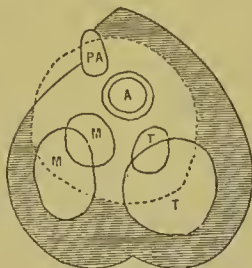


Fig. 53.

A, aorta; PA, pulmonary artery; M, mitral, and T tricuspid orifice.

give rise to incompetency of these valves, without the valves themselves being diseased (*Macalister*).]

[In order to account for the vertical diameter remaining unchanged, we may represent the ventricular fibres as consisting of three layers, viz., an inner and outer set, more or less longitudinal, and a middle set, circular. Both sets will tend, when they contract, to diminish the cavity, but the shortening of the longitudinal layers is compensated for by the

contraction, *i.e.*, the elongation produced by the circular set.]

[In order to obtain the **shape of the cavities**, dogs were taken of the same litter and as nearly alike as possible. One heart was filled with blood, as already described, and placed in a cool solution of potassic bichromate, whereby it was slowly hardened in the diastolic form, while the other was plunged as before into a hot solution. Casts were then made of the cavities.]

51. THE TIME OF THE CARDIAC MOVEMENTS.—**Methods.**—The time occupied by the various *phases of the movements* of the heart may be determined by studying the apex-beat curve.

(1) If we know at what rate the plate on which the curve was obtained moved during the experiment, of course all that is necessary is to measure the distance, and so calculate the time occupied by any event (see Pulse, § 67).

(2) It is preferable, however, to cause a tuning-fork, whose rate of vibration is known, to write its vibrations under the curve of the apex-beat (fig. 49, 2), or the curve may be written upon a plate attached to a vibrating tuning-fork (fig. 47, D, E). Such a curve contains fine teeth caused by the vibrations of the tuning-fork. D and E are curves obtained from the cardiac impulse in this way from healthy students. In D the notch *d* is not indicated. Each complete vibration of the tuning-fork, reckoned from apex to apex of the teeth = 0.01613 second, so that it is simply necessary to count the number of teeth and multiply to obtain the time. The values obtained vary within certain limits even in health.

The value of $a b$ = **pause + contraction of the auricles**, is subject to the greatest variation, and depends chiefly upon the number of heart-beats per minute. The more quickly the heart beats, the shorter is the pause, and conversely. In some curves, even when the heart beats slowly, it is scarcely possible to distinguish the auricular contraction (indicated by a rise) from the part of the curve corresponding to the pause (indicated by a horizontal line). In one case (heart-beats 55 per minute) the pause = 0.4 second, the auricular contraction = 0.177 second. In fig. 47, A, the time occupied by the pause + the auricular contraction (74 beats per minute) = 0.5 second. In D, $a b$ = 19 to 20 vibrations = 0.32 second; in E = 26 vibrations = 0.42 second.

The **ventricular systole** is calculated from the beginning of the contraction *b*, to *c*, when the semi-lunar valves are closed; it lasts from the first to the second sound. It also varies somewhat, but is more constant. When the heart beats rapidly, it is somewhat shorter—during slow action longer. In E = 0.32 second; in D = 0.29 second; with 55 beats per minute Landois found it = 0.34, with a very high rate of beating = 0.199 second.

When the ventricles beat feebly, they contract more slowly, as can be shown by applying the registering apparatus to the heart of an animal just killed. In fig. 54, from the ventricle of a rabbit just killed, the slow heart-beats, B, are seen to last longest. In cases of enormous

hypertrophy and dilatation of the left ventricle, the duration of the ventricular systole is not longer than normal (*Landois*).

In calculating the time occupied by the ventricular systole we must remember—(1) *The time*



Fig. 54.

Curves recorded by the ventricle of a rabbit upon a vibrating plate attached to a tuning-fork (vibration = 0.01613 sec.). A, soon after death; B, from the dying ventricle.

between the two sounds of the heart, *i.e.*, from the beginning of the first to the end of the second sound (*b* to *e*). (2) *The time the blood flows into the aorta*, which comes to an end at the depression between *e* and *d* (in fig. 47, E). Its commencement, however, does not coincide with *b*, as the aortic valves open 0.085 to 0.073 second after the beginning of the ventricular systole. Hence the aortic current lasts 0.08 to 0.09 second. This is calculated in the following way:—The time between the first sound of the heart and the pulse in the axillary artery is 0.137 second, and of this time 0.052 second is occupied in the propagation of the pulse-wave along the 30 cm. of artery lying between the root of the aorta and the axilla. Thus the pulse-wave in the aorta occurs 0.137 minus 0.052 = 0.085 second after the beginning of the first sound. The current in the pulmonary artery is interrupted in the depression between *d* and *e*. (3) *Lastly, the time occupied by the muscular contraction of the ventricle*, which begins at *b*, reaches its greatest extent at *e*, and is completely relaxed at *f*. The apex of the curve, *e*, may be higher or lower according to the flexibility of the intercostal space, hence the position of *e* varies. In hypertrophy with dilatation of the left ventricle, the duration of the ventricular contraction does not greatly exceed the normal.

The time which elapses between *d* and *e*—*i.e.*, between the complete closure of the aortic and pulmonary valves—is greater the more the pressure in the aorta exceeds that in the pulmonary artery, as the valves are closed by the pressure from above, and the difference in time may be 0.05 second, or even double that time, in which case the second sound appears double (compare § 54). If the aortic pressure diminishes while that in the pulmonary artery rises, *d* and *e* may be so near each other that they are no longer marked as distinct elements in the curve.

The time, *ef*, during which the ventricles relax varies somewhat: 0.1 second may be taken as a mean.

Accelerated Cardiac Action.—When the action of the heart is greatly accelerated, the pause is considerably shortened in the first instance (*Donders*), and to a less extent the time of contraction of the auricles and ventricles. When the pulse-rate is very rapid, the systole of the atria coincides with the closure of the arterial valves of the preceding contraction, as is shown in fig. 47, C (dog).

In registering the cardiac impulse, the apparatus is separated by a greater or less depth of soft parts from the heart itself, so that in all cases the intercostal tissues do not follow exactly the movements of the heart, and thus the curve obtained may not coincide mathematically with the movements of the heart. It is desirable that curves be obtained from persons whose hearts are exposed, *i.e.*, in cases of *ectopia cordis* (fig. 49, 1).

Cleft Sternum.—Gibson inserted cardiograms from the heart of a man with cleft sternum. The following were the results obtained:—Auricular contraction = 0.115; ventricular contraction (*b*, *d*) = 0.028; difference between closure of valves (*d*, *e*) = 0.09; ventricular diastole (*e*, *f*) = 0.11; pause = 0.45 second (§ 48).

Endocardial Pressure.—In large mammals, such as the horse, Chauveau and Marey (1861) determined the duration of the events that occur within the heart, and also the endocardial pressure, by means of a **cardiac sound** (fig. 56). Small elastic bags attached to tubes were introduced through the jugular vein into the right auricle and ventricle. Each of these tubes was connected with a registering tambour (fig. 55), and simultaneous tracings of the variations of pressure within the cavities of the heart were obtained by causing the writing-points of the levers

of the tambours to write upon a revolving cylinder. [This method is better adapted for showing the sequence of events than for measuring the actual endocardial pressure during the several phases of a cardiac cycle.]

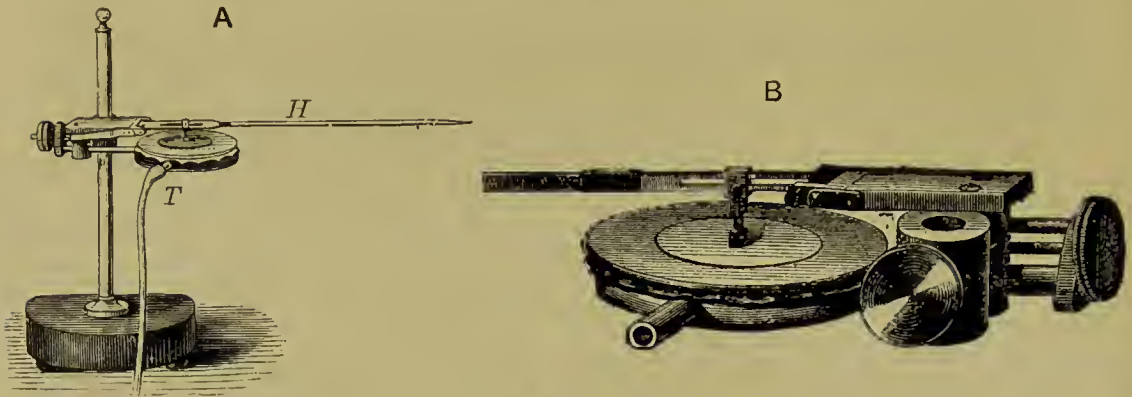


Fig. 55.

A. Marey's registering tambour. *T*, metallic capsule, with thin india-rubber stretched over it and bearing an aluminium disc, which acts upon the writing lever, *H*. By means of a thick-walled caoutchouc tube, it may be connected with any system containing air, so as to record variations of pressure. B. Natural size of the tambour, *T*.

[Marey's Cardiac Sound.—The sound (fig. 56, upper fig.) was introduced through the jugular vein into the heart until the elastic ampulla *V*, covered with thin india-rubber, came to be in the right ventricle, and *O* in the right auricle. The middle figure shows a section of the upper one, and how the ampulla *V* was connected to a tambour by means of the tube *TV*, and the ball *O* to another similar tambour by the tube *TO*.]

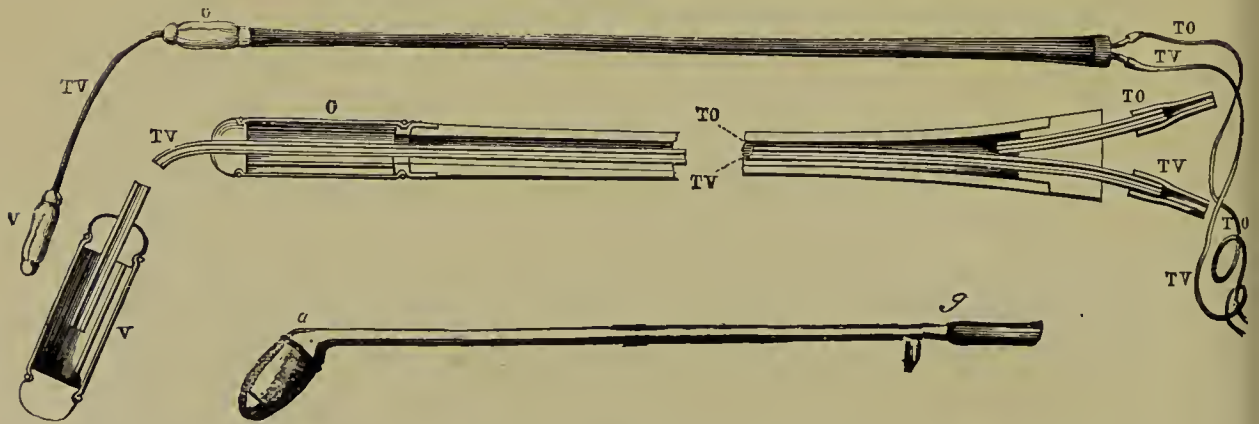


Fig. 56.

The upper and middle diagrams represent Marey's sound, the middle figure showing a section of the upper one. The lowest (*a*) is a simple cardiac sound. The bulbous portion is covered with thin india-rubber stretched over an open metallic framework so as to form an elastic bag or ampulla. By means of the tube (*g*) it can be introduced into cavity.

Fig. 57, A, gives the result obtained when one elastic bag was placed in the right auricle, being introduced through the jugular vein and superior vena cava; B, when the other bag pushed through the tricuspid orifice was in the right ventricle; D, in the root of the aorta, pushed in through the carotid; C, pushed past the semi-lunar valves into the left ventricle; while at E a similar bag has been placed externally between the heart's apex and the inner wall of the chest. In all cases *v*=auricular contraction; *V*, that of the ventricle; *s*, closure of semi-lunar valves, sooner in C than B; *P*=pause.

Methods.—(1) The cardiac sound consists of a tube containing two separate air-passages, and in connection with each of these there is a small elastic bag or ampulla. One of the bags is fixed to the free end of the sound, and communicates with one of the air-passages (fig. 56). The other bag is placed in connection with the second air-passage in the sound, and at such a distance

that when the former bag lies within the ventricle, the latter is in the auricle. Each bag and air tube communicating with it is connected with a Marey's tambour (fig. 55), provided with a lever which inscribes its movements upon a revolving cylinder. Any variation of pressure within the auricle or ventricle will affect the elastic ampullæ, and thus raise or depress the lever. Care must be taken that the writing points of the levers are placed exactly above each other. A tracing of the cardiac impulse is taken simultaneously by means of a cardiograph attached to a separate tambour.

It has still to be determined whether the auricles and ventricles act alternately, so that at the moment of the beginning of the ventricular contraction the auricles

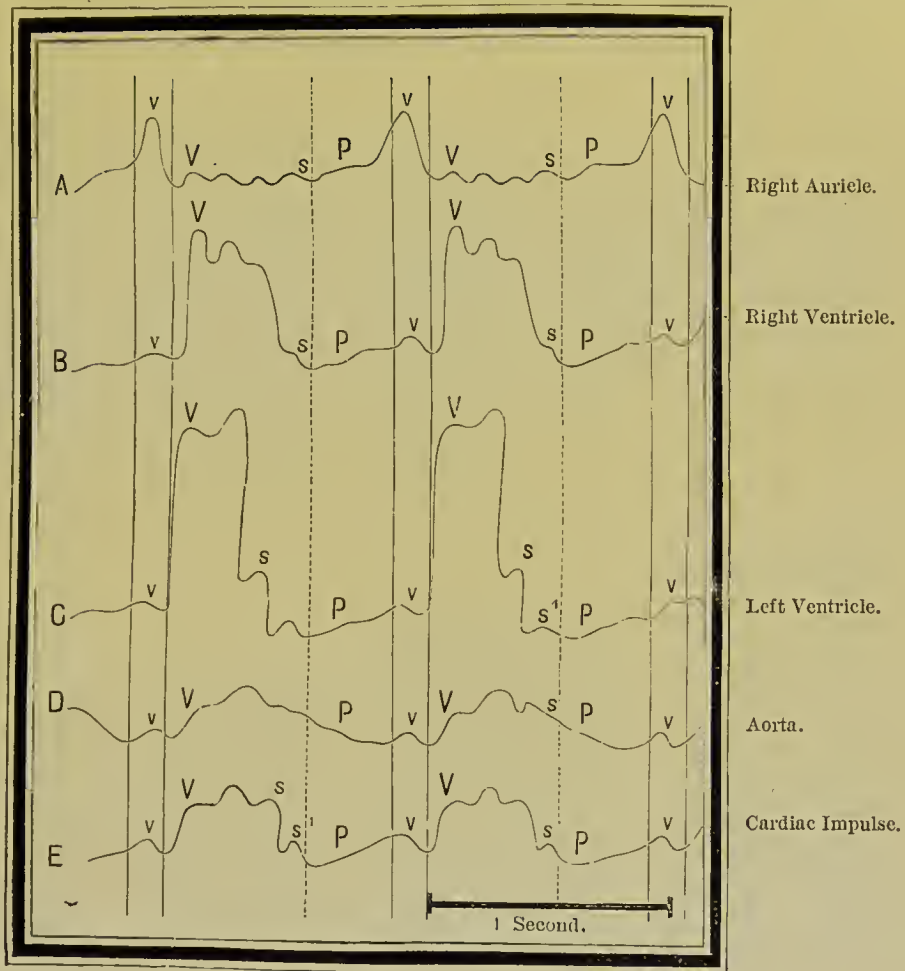


Fig. 57.

Curves obtained from the heart of a horse by the cardiac sound.

relax, or whether the ventricles are contracted while the auricles still remain slightly contracted, so that the whole heart is contracted for a short time at least. The latter view was supported by Harvey, Donders, and others, while Haller and many of the more recent observers support the view that the action of the auricles and ventricles alternates. In the case of Frau Serafin, whose heart was exposed, v. Ziemssen obtained curves from the auricles, which showed that the contraction of the auricles continued even after the commencement of the ventricular systole. In Marey's curve the contraction of the ventricle is represented as following that of the auricle (fig. 57).

(2) [The pressure within the heart has also been measured by means of the **maximum and minimum manometer** (p. 68). In the dog the maximum positive

pressure in the left ventricle is during systole greater than that in the aorta, and may reach 140 mm. Hg—that in the right ventricle 60 mm., and the right auricle about 20 mm. Hg. The minimum manometer, however, during the diastole of the ventricles records a negative pressure of -52 to -20 mm. Hg in the left and -16 mm. in the right ventricle, and -7 mm. in the right auricle.

Even after the chest is opened, the negative pressure in the left ventricle may fall as low as -25 mm. Hg.]

[(3) **Method of Rolleston and Roy.**—These observers used a special apparatus which was connected with the interior of the heart, and they find that there is no distinct rise of pressure in the dog within the ventricles corresponding to the auricular systole such as was obtained by Marey in the horse. During the ventricular diastole in certain cases the pressure falls below the atmospheric pressure and may be equal to -20 mm. mercury or more in the left ventricle (§ 48). It is probably caused by the elastic expansion of the ventricle continuing after the blood in the auricle at the moment of the cessation of the ventricular systole has entered the ventricle—*i.e.*, the quantity of blood in the auricle is not sufficient in all cases to distend the left ventricle to the point at which its suction action ceases. Magini, operating on dogs with a trocar which perforated the cavities of the heart, found none of the secondary elevations obtained by Marey with his sound. There is considerable difficulty in interpreting the curves obtained (fig. 50, B).]

A. Fick regards the alternating contraction as a means whereby the pressure in the large venous trunks is kept nearly constant. At the moment of ventricular systole the auricles relax, and the venous blood flows freely into the latter, while if the auricles remained contracted, the blood in the veins would be kept back. Further, at the moment of ventricular diastole the auricles contract, so that there is not an abnormal diminution of the pressure in the veins. Thus the pressure in the auricle is more equable, while the current in the terminal parts of the veins is kept more constant.

52. PATHOLOGICAL CARDIAC IMPULSES.—Change in the Position of the Apex-Beat.—The position of the cardiac impulse is changed—(1) by the accumulation of fluids (serum, pus, blood) or gas in one pleural cavity. A copious effusion into the left pleural cavity compresses the lung, and may displace the heart towards the right side, while effusion on the right side may push the heart more to the left. As the right heart must make a greater effort to propel the blood through the compressed lung, the cardiac impulse is usually increased. Advanced emphysema of the lung, causing the diaphragm to be pressed downwards, displaces the heart downwards and inwards, while pushing and pulling up of the diaphragm (by contraction of the lung, or through pressure from below) causes the apex-beat to be displaced upwards, and also slightly to the left. Thickening of the muscular walls with dilatation of the cavities of the left ventricle makes that ventricle longer and broader, while the increased cardiac impulse may be felt in the axillary line in the sixth, seventh, or even eighth intercostal space to the left of the mammary line. Hypertrophy, with dilatation of the right side, increases the breadth of the heart, so that the cardiac impulse is felt more to the right, even to the right of the sternum. In the rare cases where the heart is transposed, the apex-beat is felt on the right side. When the cardiac impulse goes to the left of the left mammary line, or to the right of the parasternal line, the heart is increased in breadth, and there is hypertrophy of the heart. A greatly increased cardiac impulse may extend to several intercostal spaces.

The cardiac impulse is abnormally **weakened** in cases of atrophy and degeneration of the cardiac muscle, or by weakening of the innervation of the cardiac ganglia. It is also weakened when the heart is separated from the chest-wall owing to the collection of fluids or air in the pericardium, or by a greatly distended left lung; and, indeed, when the left side of the chest is filled with fluid, the cardiac impulse may be extinguished. The same occurs when the left ventricle is very imperfectly filled during its contraction (in consequence of marked narrowing of the mitral orifice), or when it can only empty itself very slowly and gradually, as during marked narrowing of the aortic orifice.

An **increase** of the cardiac impulse occurs during hypertrophy of the walls, as well as under the influence of various stimuli (psychical, inflammatory, febrile, toxic) which affect the cardiac ganglia. Great hypertrophy of the left ventricle causes the heart to *heave*, so that a part of the left chest-wall may be raised and also vibrate during systole.

A **pulling in** of the anterior wall of the chest during the cardiac systole occurs in the third and fourth interspaces, not unfrequently under normal circumstances, sometimes during increased cardiac action, and in eccentric hypertrophy of the ventricles. As the heart's apex is slightly displaced, and the ventricle becomes slightly smaller during its systole, the empty space is filled by the yielding soft parts of the intercostal space. When the heart is united with the pericardium and the surrounding connective-tissue, which renders systolic locomotion of the heart impossible, retraction of the chest-wall during systole takes the place of the

cardiac impulse (*Skoda*). During the diastole, a diastolic cardiac impulse of the corresponding part of the chest-wall may be said to occur.

Clinically, changes in the cardiac impulse are best ascertained by taking graphic representations of the cardiac impulse, and studying the curves so obtained (fig. 58).

In curve P (much reduced), from a case of marked **hypertrophy with dilatation**, the ventricular contraction, *bc*, is usually very great, while the time occupied by the contraction is not much increased. P and Q were obtained from a case of marked **eccentric hypertrophy** of the left ventricle, due to insufficiency of the aortic valves. Curve Q was taken intentionally over the auriculo-ventricular groove, where retraction of the chest-wall occurred during systole; nevertheless the individual events occurring in the heart are indicated.

Fig. E is from a case of **aortic stenosis**. The auricular contraction (*ab*) lasts only a short time; the ventricular systole is obviously lengthened, and after a short elevation (*bc*) shows a

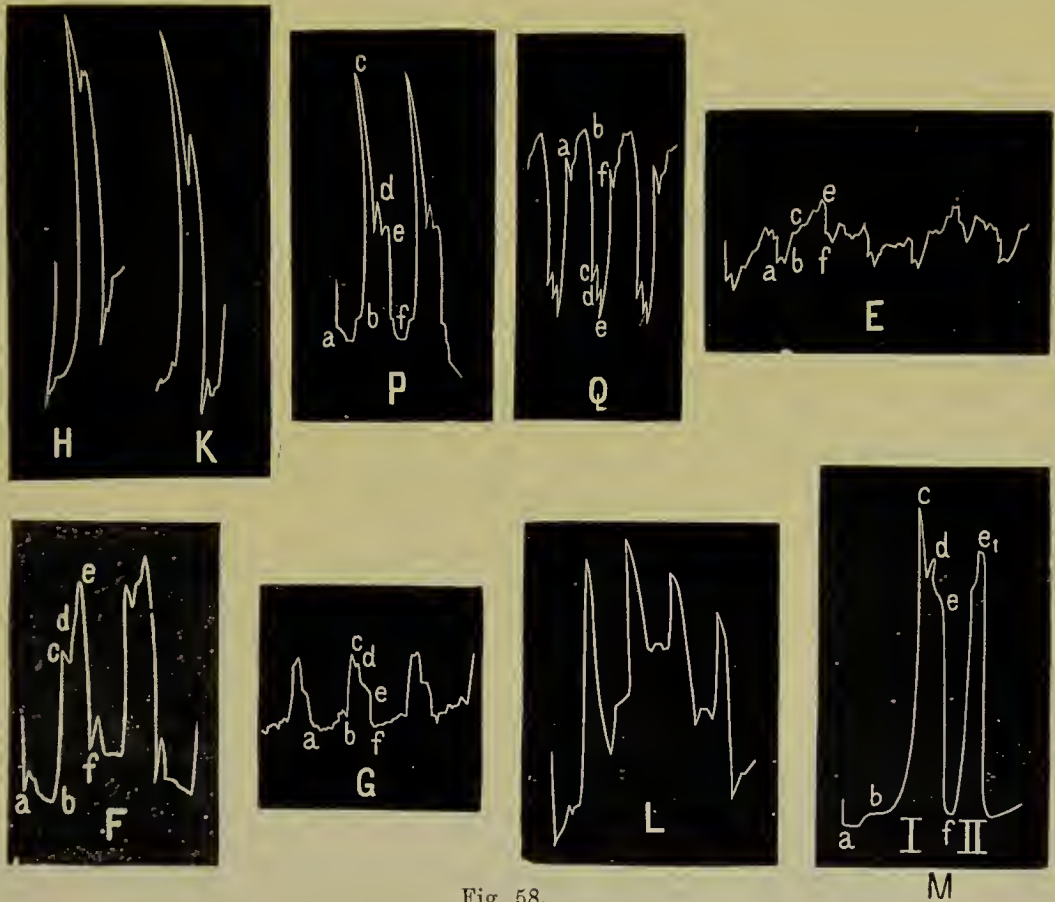


Fig. 58.

Curves of the cardiac impulse. *ab*, contraction of auricles; *bc*, ventricular systole; *d*, closure of aortic, and *e*, of pulmonary valves; *ef*, diastole of ventricle; P, Q, hypertrophy and dilatation of the left ventricle; E, stenosis of the aortic orifice; F, mitral insufficiency; G, mitral stenosis; L, nervous palpitation in Basedow's disease; M, so-called hemisystole.

series of fine indentations (*c, e*) caused by the blood being pressed through the narrowed and roughened aorta.

Fig. F, from a case of **insufficiency of the mitral valve**, shows (*ab*) well marked on account of the increased activity of the left auricle, while the shock (*d*) from the closure of the aortic valves is small, on account of the diminished arterial tension. On the other hand, the shock from the accentuated pulmonary sound (*e*) is very great, and is in the apex of the curve. On account of the great tension in the pulmonary artery, the second pulmonary tone may be so strong, and succeed the second aortic sound (*d*) so rapidly, that both almost merge completely into each other (H and K).

The curve of **stenosis of the mitral orifice** (G) shows a long, irregular, notched, auricular contraction (*ab*), caused by the blood being forced through an irregular narrow orifice. The ven-

tricular contraction (*bc*) is feeble because the ventricle is imperfectly filled. The closures of the two valves, *d* and *e*, are relatively far apart, and one can hear distinctly a reduplicated second sound. The aortic valves close rapidly, because the aorta is imperfectly supplied with blood, while the more copious inflow of blood into the pulmonary artery causes its valves to close later.

If the heart beats rapidly and feebly—if the blood-pressure in the aorta and pulmonary artery be low, the signs of closure of the pulmonary valves may be absent—as in curve L—taken from a girl suffering from nervous palpitation and morbus Basedowii.

In very rare cases of insufficiency of the mitral valve, it has been observed that at certain times both ventricles contract simultaneously, as in a normal heart, but that this alternates with a condition where the right ventricle alone seems to contract. Curve M is such a curve obtained by Malbranc, who called this condition **intermittent hemisystole**. The first curve (I.) is like a normal curve, during which the whole heart acted as usual. The curve II., however, is caused by the right side of the heart alone; it wants the closure of the aortic valves *d*, and there was no pulse in the arteries. Owing to insufficiency of the tricuspid valve, the same person had a venous pulse with every cardiac impulse, so that the arterial and venous pulses first occurred together and then the venous pulse alone occurred. In these cases the mitral insufficiency leads to the right ventricle being over-distended, while the left is nearly empty, so that the right side requires to contract more energetically than the left. It does not seem that the right ventricle alone contracts in these cases, but rather that the action of the left side is very feeble.

53. THE HEART-SOUNDS.—On listening over the region of the heart in a healthy man, either with the ear applied directly to the chest-wall (*Harvey*), or by means of a stethoscope (*Laennec*, 1819), we hear two characteristic sounds, the so-called “**heart-sounds**.” The **two sounds** are called first and second, and together they correspond to a single cardiac cycle. These sounds are separated by silences. [Fig. 59 shows the relation of the events occurring in the heart during a cardiac cycle to the sounds and silences.]

1. The first sound.
2. The first or short silence.
3. The second sound.
4. The second or long silence.

[**Relative Duration.**—There is no absolute duration of each phase of a cardiac cycle, but we may take the average relative duration calculated from the measurements of Gibson, in a case of fissure of the sternum, to be as follows:—



Fig. 59.

Scheme of a cardiac cycle. The inner circle shows what events occur in the heart, and the outer, the relation of the sounds and silences to these events.

Auricular systole, ...	·112 sec.
Ventricular systole, ...	·368 „
Ventricular diastole, ...	·578 „

Cardiac cycle, ... 1·058 sec.

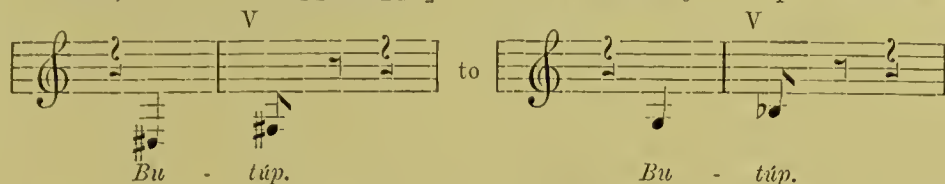
Suppose we divide the cycle into tenths (*Walshe*), then the first sound will last $\frac{4}{10}$, the first silence $\frac{1}{10}$, the second sound $\frac{2}{10}$, and the long silence $\frac{3}{10}$ of the entire period.]

The **first sound** [long or systolic] is twice as long as, somewhat duller, and one-third or one-fourth deeper, than the second sound; it is less sharply defined at first, and is *synchronous with the systole of the ventricles*.

The **second sound** [short or diastolic] is clearer, sharper, shorter, more sudden, and is one-third to one-fourth higher in pitch; it is sharply defined and *synchronous with the closure of the semi-lunar valves*. It marks the beginning of ventricular diastole. The sounds

emitted during each cardiac cycle have been compared to the pronunciation of the syllables *lubb*, *düpp*. [If one listens over the apex one hears the sounds like

lúpp, *dupp*; where the accent is on the first sound, but at the base, it is on the second sound, and is like *lupp*, *dúpp*.] Or the result may be expressed thus:—



[It is to be remembered that in reality *four* sounds are produced in the heart, but the two first sounds occur together and the two second, so that only a single first and a single second sound are heard.]

The **causes of the first sound** are due to two conditions. As the sound is heard, although enfeebled, in an excised heart in which the movements of the valves are arrested, and also when the finger is introduced into the auriculo-ventricular orifices so as to prevent the closure of the valves (*C. Ludwig and Dogiel*), one of the factors lies in the “*muscle sound*” produced by the contracting muscular fibres of the ventricles. This sound is supported and increased by the sound produced by the tension and vibration of the auriculo-ventricular valves and their chordæ tendineæ, at the moment of the ventricular systole. Wintrich, by means of proper resonators, has analysed the first sound and distinguished the clear, short, valvular part from the deep, long, muscular sound.

[Krehl has made additional experiments to show that the first sound is partly muscular. An apparatus was devised whereby, while the heart was still within the body and the circulation going on, modifications of the first sound were obtained when the auriculo-ventricular valves were held apart. Again, when a dog is bled from the carotids, as soon as a considerable amount of blood is removed, the second sound is no longer heard, while the first sound lasts for some time longer and is even fairly loud. It is also said that the auricles produce a sound during their contraction. Kasem-Beck has also recently confirmed Dogiel's previous statements and supported them by new experiments.]

The muscle-sound produced by *transversely-striped muscle* does not occur with a *simple* contraction (p. 99), but only when several contractions are superposed to produce tetanus (§ 303). The ventricular contraction is only a *simple* contraction, but it lasts considerably longer than the contraction of other muscles, and herein lies the cause of the occurrence of the muscle-sound during the ventricular contraction.

Defective Heart-Sounds.—In certain conditions (typhus, fatty degeneration of the heart), where the muscular substance of the heart is much weakened, the first sound may be completely inaudible. In aortic insufficiency, in consequence of the reflux of blood from the aorta into the ventricle, the mitral valve is gradually stretched, and sometimes even before the beginning of the ventricular systole, the first sound may be absent. Such pathological conditions seem to show that, for the production of the first sound, muscle-sound and valve-sound must eventually work together, and that the tone is altered, or may even disappear, when one of these causes is absent. [Yeo and Barrett state that the sound is purely muscular (?).]

The cause of the second sound is undoubtedly due to the prompt closure, and therefore sudden stretching or tension, of the semi-lunar valves of the aorta and pulmonary artery, so that it is purely a valvular sound. Perhaps it is augmented by the sudden vibration of the fluid-particles in the large arterial trunks. [The second sound has all the characters of a valvular sound. That the aortic valves are concerned in its production was proved by Hope, who introduced a curved wire through the left carotid artery and hooked up one or more segments of the valve, when the sound was modified. It may even disappear or be replaced by an abnormal sound or “murmur.” Again, when these valves are diseased, the sound is altered, and it may be accompanied or even displaced by murmurs.] Although the aortic and pulmonary valves do not close simultaneously, usually the difference in time is so small that *both* valves make *one* sound, but the second sound may be double or divided when, through increase of the difference of pressure in the aorta and pulmonary artery, the interval becomes longer. Even in health this may be the case, as occurs at the end of inspiration or the beginning of expiration (*v. Dusch*).

Where the Sounds are Heard Loudest.—[Clinicians, for convenience, in describing the cardiac sounds as heard on auscultation speak of four areas, viz.: the *mitral area*, a circular area about 2 inches in diameter, with the apex as a centre; the *tricuspid area*, from the third to the fifth interspaces on the left side, and the adjoining part of the sternum; the *aortic area*, second right interspace near the sternum, or the *inner* end of the second costal cartilage; the *pulmonary area*, the inner end of the second left intercostal space. The *first sound* is heard best at the apex, and much fainter at the base. The *second sound* is heard best over the base.] The sound produced by the *tricuspid valve* is heard loudest at the junction of the lower right costal cartilages with the sternum; as the *mitral valve* lies more to the left and deeper in the chest, and is covered in front by the arterial orifice, the mitral sound is best heard at the apex-beat, or immediately above it, where a strip of the left ventricle lies next the chest-wall. [The sound is conducted to the part nearest the ear of the listener by the muscular substance of the heart.] The aortic and pulmonary orifices lie so close together that it is convenient to listen for the second (*aortic*) sound in the direction of the aorta, where it comes nearest to the surface, *i.e.*, over the second right costal cartilage or aortic cartilage close to its junction with the sternum. The sound, although produced at the semi-lunar valves, is carried upwards by the column of blood, and by the walls of the aorta. The sound produced by the *pulmonary artery* is heard most distinctly over the end of the second right intercostal space, or the third left costal cartilage, somewhat to the left and external to the margin of the sternum (fig. 60).

[It is important to remember that the *position of the cardiac valves* is one thing, and the situation where the heart-sounds are heard loudest is another. The following indicates the topographical arrangement of the orifices:—

Aortic orifice.—At the sternum adjoining the third left cartilage and space.

Pulmonary orifice.—Second left space and sternum adjoining.

Mitral orifice.—Left half of sternum from fourth to fifth cartilage.

Tricuspid orifice.—Right half of sternum from fourth to sixth cartilage.

The aortic and mitral orifices are deeply situated in the chest, while the pulmonary and tricuspid orifices are comparatively superficial.]

[Events occurring in the **heart during the sounds.**—Coincident with the **first sound** the following events are taking place within the heart:—(1) Contraction of both ventricles, (2) firmer closure and stretching of the auriculo-ventricular valves, (3) propulsion and rushing of blood into the aorta and pulmonary artery, (4) the impulse of the heart against the chest-wall, (5) the gradual filling of the auricles with blood. Coincident with the **second sound** are—(1) the closure and stretching of the semi-lunar valves of the aorta and pulmonary artery, (2) relaxation of the contracted ventricles, (3) opening of the auriculo-ventricular valves and flow of some blood from the auricles into the ventricles, (4) diminished pressure of the apex against the chest-wall. During the **long pause**:—(1) The auricles are being filled, and blood flows freely from them into the dilated ventricles, (2) contraction of the auricles to fill the ventricles with blood.] During the short silence, which is very short, the ventricles are contracting, and are near their maximum of shortening.

54. VARIATIONS OF THE HEART-SOUNDS.—Increase of the first sound of both ventricles indicates a more energetic contraction of the ventricles and a simultaneously greater and more sudden tension of the auriculo-ventricular valves. Increase of the second sound is a sign of increased tension in the interior of the corresponding large arteries. Hence increase of the second (pulmonary) sound indicates overfilling and excessive tension in the pulmonary circuit. A feeble action of the heart, as well as abnormal want of blood in the heart, causes weak heart-sounds, which is the case in degenerations of the heart-muscle.

Irregularities in structure of the individual valves may cause the heart-sounds to become "impure." If a pathological cavity, filled with air, be so placed, and of such a form as to act

as a resonator to the heart-sounds, they may assume a "metallic" character. The first and second sound may be "reduplicated" or [although "duplication" is a more accurate term (*Barr*)] doubled. The reduplication of the first sound is explained by the tension of the tricuspid and that of the mitral valves not occurring simultaneously. Sometimes in disease a

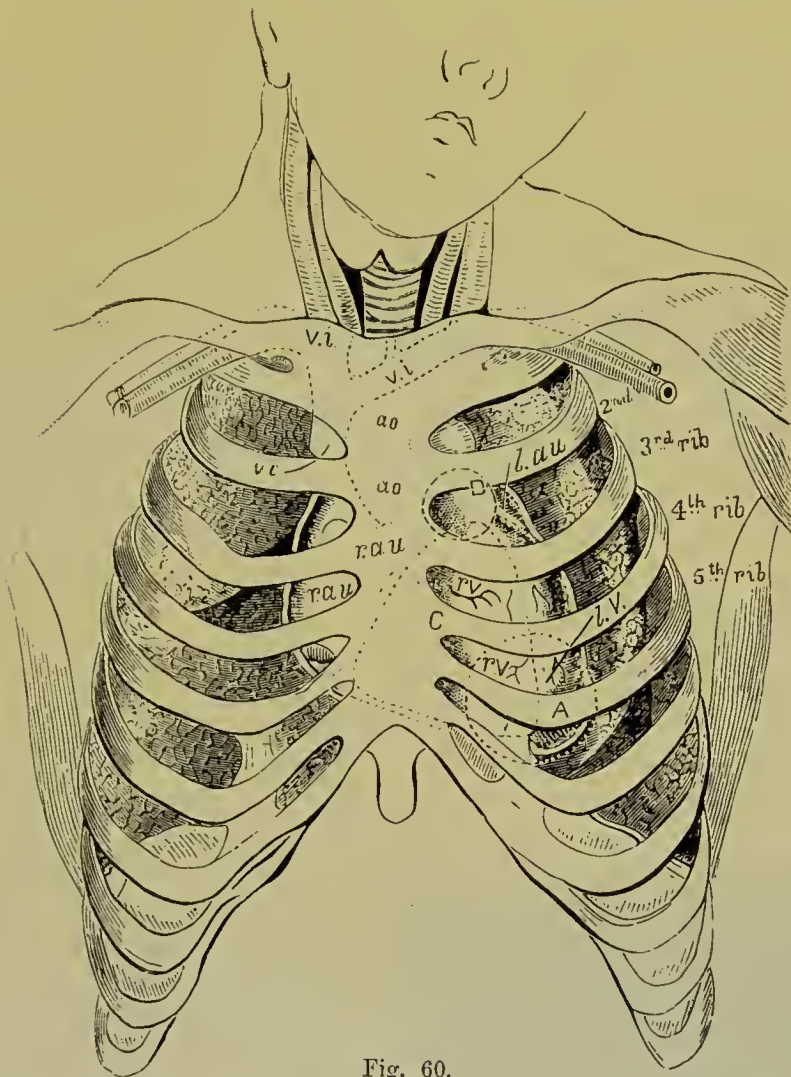


Fig. 60.

The heart—its several parts and great vessels in relation to the front of the thorax. The lungs are collapsed to their normal extent, as after death, exposing the heart. The outlines of the several parts of the heart are indicated by very fine dotted lines. The area of propagation of valvular murmurs is marked out by more visible dotted lines. A, the circle of mitral murmur, corresponds to the left apex. The broad and somewhat *diffused* area, roughly triangular, is the region of tricuspid murmurs, and corresponds generally with the right ventricle, where it is least covered by lung. The letter C is in its centre. The circumscribed *circular area*, D, is the part over which the pulmonic arterial murmurs are commonly heard loudest. In many cases it is an inch, or even more, lower down, corresponding to the *conus arteriosus* of the right ventricle, where it touches the wall of the thorax. The internal organs and parts of organs are indicated by letters as follows:—*r.au*, right auricle, traced in fine dotting; *ao*, arch of aorta, seen in the first intercostal space, and traced in fine dotting on the sternum; *v.i.*, the two innominate veins; *r.v.*, right ventricle; *l.v.*, left ventricle.

sound is produced by a hypertrophied auricle producing an audible *presystolic* sound, *i.e.*, a sound or "murmur" preceding the first sound. [This has been questioned quite recently.] As the aortic and pulmonary valves do not close quite simultaneously, a *reduplicated second sound*

is only an increase of a physiological condition. All conditions which cause the aortic valves to close rapidly (diminished amount of blood in the left ventricle) and the pulmonary valves to close later (congestion of the right ventricle—both conditions together in mitral stenosis), favour the production of a reduplicated second sound.

Cardiac Murmurs.—If irregularities occur in the valves, either in cases of stenosis or in insufficiency, so that the blood is subjected to vibratory oscillations and friction, then, instead of the heart-sounds, other sounds—**murmurs** or **bruits**—arise or accompany these. A combination of these sounds is always accompanied by disturbances of the circulation. [These murmurs may be produced within the heart, when they are termed **endocardial**; or outside it, when they are called **exocardial** murmurs. But other murmurs are due to changes in the quality or amount of the blood, when they are spoken of as **hæmic** murmurs. In the study of all murmurs, note their *rhythm* or exact relation to the normal sounds, their *point of maximum intensity*, and the *direction in which the murmur is propagated*.] It is rare that tumours or other deposits projecting into the ventricles cause murmurs, unless there be present at the same time lesions of the valves and disturbances of the circulation. The cardiac murmurs are always related to the systole or diastole, and usually the systolic are more accentuated and louder. Sometimes they are so loud that the thorax trembles under their irregular oscillations (*fremitus*, *frémissement cataire*).

In cases where **diastolic murmurs** are heard, there are always anatomical changes in the cardiac mechanism. These are insufficiency of the arterial valves, or stenosis of the auriculo-ventricular orifice (usually the left). **Systolic murmurs** do not always necessitate a disturbance in the cardiac mechanism. They may occur on the left side, owing to insufficiency of the mitral valve, stenosis of the aorta, and in cases of calcification and dilatation of the ascending part of the aorta. These murmurs occur very much less frequently on the right side, and are due to insufficiency of the tricuspid and stenosis of the pulmonary orifice.

Functional Murmurs.—Systolic murmurs often occur without any valvular lesion, although they are always less loud, and are caused by abnormal vibrations of the valves or arterial walls. They occur most frequently at the orifice of the pulmonary artery [and are generally heard at the base], less frequently at the mitral, and still less frequently at the aortic or the tricuspid orifice. Anæmia, general malnutrition, acute febrile affections, are the causes of these murmurs. [Some of these are due to an altered condition of the blood, and are called **hæmic**, and others to defective cardiac muscular nutrition, and are called **dynamic** (*Walshe*).]

Sounds may also occur during a certain stage of inflammation of the pericardium (pericarditis) from the roughened surfaces of this membrane rubbing upon each other. Audible friction sounds are thus produced, and the vibration may even be perceptible to touch. [These are "**friction sounds**," and quite distinct from sounds produced within the heart itself.]

55. PERSISTENCE OF THE MOVEMENTS OF THE HEART.—The heart continues to beat for some time after it is cut out of the body. The movement

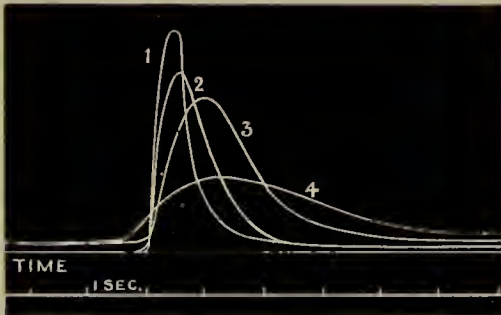


Fig. 61.

Curves of excised rabbit's heart—1, 6 mins. after excision; 2, 10 mins.; 3, 20 mins.; 4, 70 mins. (after *Waller and Reid*).

lasts longer in cold-blooded animals (frog, turtle)—extending even to days—than in mammals. A rabbit's heart beats from 3 minutes up to 36 minutes after it is cut out of the body. The average of many experiments is about 11 minutes. [Waller and Reid recorded the ventricular contractions of a rabbit's heart 72 minutes after its excision. Fig. 61 shows the prolongation of the ventricular systole in an excised rabbit's heart, the movements being recorded by a lever resting on the heart.] Panum found the last trace of contraction to occur in the right auricle (rabbit) 15 hours after death; in a mouse's heart, 46 hours; in a dog's, 96 hours. An excised frog's heart beats, at the longest, $2\frac{1}{2}$ days (*Valentin*). In a human embryo (third month) the heart was found beating after 4 hours. In this condition stimulation causes an increase and acceleration of the action. The ventricular contraction weakens, and soon each auricular contraction is not followed by a ventricular contraction, two or more of the former being succeeded by only one of the latter. At the same time the ventricles contract more slowly (fig. 61), and soon stop altogether,

while the auricles continue to beat. If the ventricles be stimulated directly, as by pricking them with a pin, they may execute a contraction. The left auricle soon ceases to beat, while the right auricle still continues to contract. The right auricular appendix continues to beat longest, as was observed by Galen and Cardanus (1550), and it is termed "ultimum moriens." Similar observations have been made upon the hearts of persons who have been executed.

If the heart has ceased to beat, it may be excited to contract for a short time by direct stimulation, more especially by heat (*Harvey*); even under these circumstances the auricles and their appendices are the last parts to cease contracting. As a general rule, direct stimulation, although it may cause the heart to act more vigorously for a short time, brings it to rest sooner. In such cases, therefore, the regular sequence of events ceases, and there is usually a twitching movement of the muscular fibres of the heart. C. Ludwig found that, even after the excitability is extinguished in the mammalian heart, it may be restored by injecting arterial blood into the coronary arteries: conversely, lesion of these vessels is followed by enfeebled action of the heart (§ 47). Hammer found that in a man, whose left coronary artery was plugged, the pulse fell from 80 to 8 beats per minute.

[The beats of the excised heart of a rabbit gradually decline in force and frequency, the latent period and contraction become longer, and the excitability more obtuse. The duration of a contraction may be .6 sec., the normal being .3 sec. The beats have often a bigeminal character. An excised heart may be frozen quite hard, yet on being thawed it contracts spontaneously. The contraction proceeds in a wave from the spot stimulated in the frog's heart, at 8° to 12° C. at 30 to 90 mm. per sec.; in the mammalian excised heart about 8 metres per sec. (*Waller and Reid*).]

Action of Gases on the Heart.—During its activity the heart uses O, and produces CO₂ so that it beats longest in pure O (12 hours), and not so long in N,—H (1 hour)—CO₂ (10 minutes)—CO (42 minutes)—Cl (2 minutes), or in a vacuum (20 to 30 minutes), even when there is watery vapour present to prevent evaporation. If the heart be reintroduced into O it begins to beat again. [Gases seem to have the same effect in the chick's heart on the second and third days of incubation as in the adult heart (*Fano*). A frog's heart ceases to beat in compressed O (10 to 12 atmospheres) in about one-third of the time it would do were it simply excised and left to itself. An excised heart suspended in ordinary air beats three to four times as long as a heart which is placed upon a glass-plate.]

[56. PHYSICAL EXAMINATION OF THE HEART.—The physical methods of diagnosis enable us to obtain precise knowledge regarding the actual state of the heart. The methods available are:—

- | | |
|----------------|------------------|
| 1. Inspection. | 3. Percussion. |
| 2. Palpation. | 4. Auscultation. |

To arrive at a correct diagnosis all the methods must be employed.]

[Inspection.—The person is supposed to have his chest exposed and to be in the recumbent position. It is important to remember the limits of the heart. The base corresponds to a line joining the upper margins of the third costal cartilages, the apex to the fifth interspace, while transversely it extends from a little to the right of the sternum to within a little of the left nipple; this area occupied by the heart being called the deep cardiac region (fig. 62). By the eye we can detect any alteration in the configuration of the præcordia, bulging or retraction of the region as a whole or of the intercostal spaces, and we may detect variations in the position, character, extent of the cardiac impulse, or the presence of other visible pulsations.]

[Palpation.—By placing the whole hand flat upon the præcordia, we can ascertain the presence or absence, the situation and extent, and any alterations in the characters of the apex-beat; or we may detect the existence of abnormal pulsations, vibrations, thrills, or friction in this region. In feeling for the apex-beat, if it be at all feeble, it is well to make the patient lean forward. Of course, it must be remembered that the whole heart may be displaced by tumours or accumulations of fluids pressing upon it, *i.e.*, conditions external to itself, or the apex-beat may be displaced from causes within the heart itself, as in hypertrophy of the left ventricle.]

[Percussion.—As the heart is a solid organ, and is surrounded by the lungs, which contain air, it is evident that the sound emitted by striking the chest over the region of the former must be different from that produced over the latter. Not only is there a difference in the

sound or note emitted, but the "sensation of resistance" which one feels on percussing the two organs is different. We may ascertain—

1. The superficial or absolute cardiac dulness.
2. The deep or relative dulness.]

[**Superficial Cardiac Dulness.**—This theoretically is the part of the heart in direct contact with the chest-wall and uncovered by lung, but obviously as the lungs vary in size during respiration, it must be smaller during inspiration and larger during expiration. It forms a roughly triangular space, whose base cannot be accurately determined, as the heart-dulness

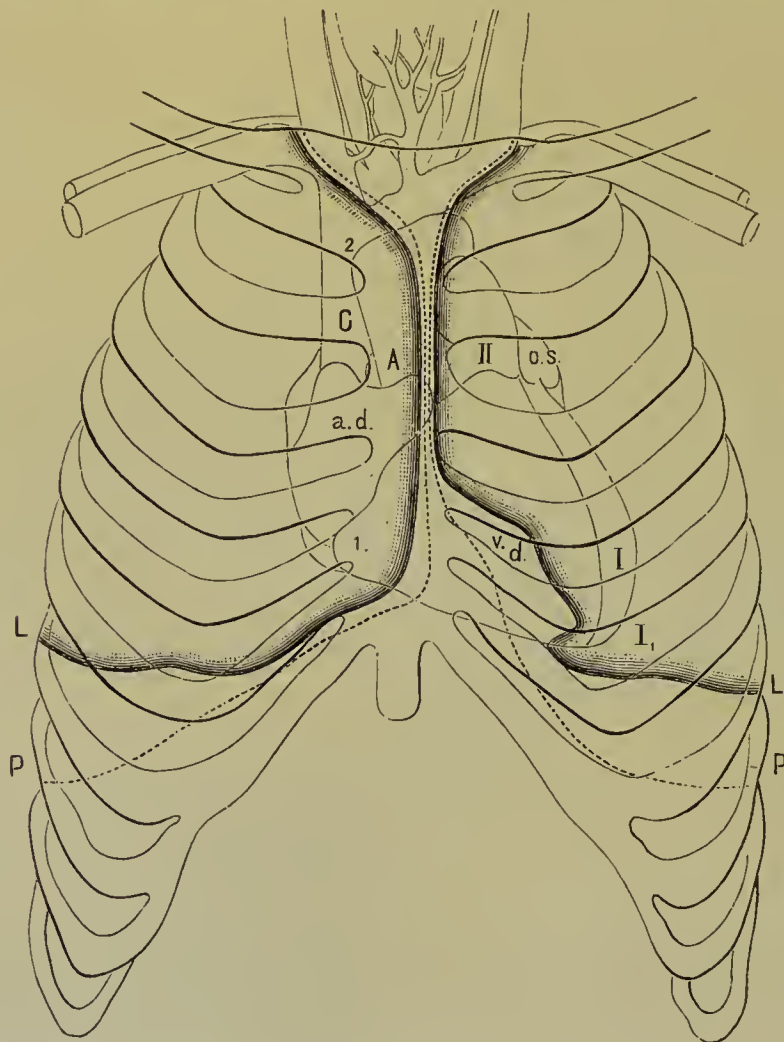


Fig. 62.

Topography of the thorax and its contents. *a.d.*, right atrium; *o.s.*, left auricle; *v.d.*, right ventricle; *I*, left ventricle, with *I*₁, position of cardiac impulse; *A*, aorta; *II*, pulmonary artery; *C*, *V*, vena cava superior; *L*, *L*, limits of the lungs; *P*, *P*, limits of the attachment of the parietal pleura; the space between *L*, *L*, and *P*, *P*, is called the "complemental space."

merges into that of the liver, situate below it, but it corresponds to a horizontal line $2\frac{1}{2}$ inches long, extending from the apex-beat to the middle of the sternum. The internal side corresponding to the left edge of the sternum is 2 inches long, and reaches from the junction of the fourth costal cartilage with the sternum—apex of the triangle—to the sternal end of the base line. The superior, outer, or oblique line, 3 inches in length, is somewhat curved, and passes downwards and outwards from the apex of the triangle to the apex of the heart. The clinical value of the superficial dulness is not great.]

[**Deep Cardiac Dulness.**—By this method theoretically we seek to define the exact limits of the heart as a whole, and thus to ascertain its absolute size, and of course percussion has to be

done through a certain thickness of lung tissue, and hence one must strike the pleximeter forcibly. It extends vertically from the third rib and ends at the sixth, but owing to the cardiac merging in the hepatic dulness, this lower limit cannot be accurately ascertained; while *transversely* at the fourth rib it extends from just within the nipple line to slightly beyond the right of the sternum. By these means we may detect increase in the size of the heart or alterations in the relation of the lungs to the heart, fluid in pericardium, &c. Thus it is of great importance to the clinician, enabling him to determine the size and position of the heart.]

[**Auscultation.**—This is one of the most valuable methods, for by it we can detect variations and modifications in the healthy sounds of the heart, the rhythm and frequency of the heart-beat, the existence of abnormal sounds, and their exact relation to the normal sounds, also their characters and relation to the cardiac cycle, and the direction in which these sounds are propagated (§ 54).]

57. INNERVATION OF THE HEART.—[**Intra- and Extra-Cardiac Nervous Mechanism.**—When the heart is removed from the body, or when all the nerves which pass to it are divided, it still beats for some time, so that its movements must depend upon some mechanism situated within itself. The ordinary rhythmical movements of the heart are undoubtedly *associated with* the presence of nerve ganglia, which exist in the substance of the heart—the *intra-cardiac ganglia*. But the movements of the heart are influenced by nervous impulses which reach it from without, so that there falls to be studied an *intra-cardiac* and an *extra-cardiac* nervous mechanism.]

The **cardiac plexus** is composed of the following nerves:—(1) The cardiac branches of the vagus, the branch of the same name from the external branch of the superior laryngeal, a branch from the inferior laryngeal, and sometimes branches from the pulmonary plexus of the vagus (more numerous on the right side); (2) the superior, middle, inferior, and lowest cardiac branches of the three cervical ganglia and the first thoracic ganglia of the sympathetic; (3) the inconstant twig of the descending branch of the hypoglossal nerve, which, according to Luschka, arises from the upper cervical ganglion. From the plexus there proceed—the *deep* and the *superficial* nerves (the latter usually at the division of the pulmonary artery under the arch of the aorta, and containing the ganglion of Wrisberg) (§ 370). The following nerves may be separately traced from the plexus:—

(a) The **plexus coronarius dexter and sinister**, which contains the *vaso-motor nerves* for the coronary vessels (physiological proof still wanting) as well as the nerves (sensory?) proceeding from them (to the pericardium?).

(b) **Intra-cardiac nerves and ganglia.**—The nerves lying in the *grooves of the heart* and in *its substance* contain numerous ganglia (*Remak*), and are regarded as the automatic motor centres of the heart. A nervous ring containing numerous ganglia corresponds to the margin of the septum atriorum; there is another in the auriculo-ventricular groove. Where the two meet, they exchange fibres. The ganglia usually lie near the pericardium. In *mammals*, the two largest ganglia lie near the orifice of the superior vena cava—in *birds*, the largest ganglion (containing thousands of ganglionic cells) lies posteriorly where the longitudinal and transverse sulci cross each other. Fine branches, also provided with small ganglia, proceed from these ganglia, and penetrate the muscular walls of the auricles and ventricles.

[**Frog's Heart.**—The frog's heart consists of the **sinus venosus**, into which open the single inferior and the two superior venæ cavae (fig. 64). There are two **auricles**; the right one communicates with the sinus venosus, and opens into the single ventricle; the left auricle also opens into the **single ventricle** (fig. 63, *v*), and in the latter are mixed the venous blood returned by the right auricle and the arterial blood from the left auricle. The aorta with its *bulbus arteriosus* conducts the blood from the ventricle. The various orifices are guarded by projections of tissue, which act like valves. The two auricles are completely separated by a septum. This septum ends posteriorly in a free concave margin, so as to divide the auriculo-ventricular orifice into a right and left orifice. Each orifice is guarded by two thick fleshy valves, which close it.]

[**Nerves.**—The two cardiac branches of the vagi—the *nervi cardiaci*—proceed to the posterior surface of the sinus venosus, and where the latter joins the auricle they interlace, and are mixed

with a number of ganglion cells (fig. 67). This spot is called **Remak's ganglion**, is sometimes single, at others double, and it can be seen as a white "crescent" when the heart is lifted up and looked at from behind (fig. 64). The cardiac nerves pass on to the auricular septum—

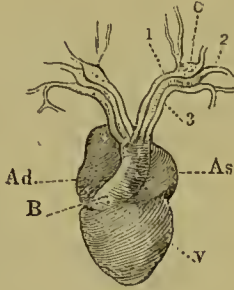


Fig. 63.

Heart of frog from the front. V, single ventricle; Ad, As, right and left auricles; B, bulbus arteriosus; 1, carotid, 2, aorta, and 3, pulmo-cutaneous arteries; C, carotid gland.

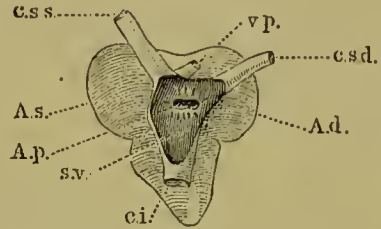


Fig. 64.

Heart of frog from behind. s.v., sinus venosus opened; ci, inferior; csd, css, right and left superior venae cavae; vp., pulmonary vein; Ad and As, right and left auricles; Ap, communication between the right and left auricle.

which contains nerve-cells, known as **Ludwig's ganglion**—exchanging fibres in their course to join two ganglia at the auriculo-ventricular groove, and known as **Bidder's ganglia** (fig. 67). It has been stated that the bulbus arteriosus also contains ganglionic cells.]



Fig. 65.

Auricular septum of a frog's heart. a, anterior, and p, posterior branch of the cardiac vagus; B, Bidder's ganglion.



Fig. 66.

Pyriform ganglionic bi-polar nerve-cell from the heart of a frog. m, sheath; n, straight process; o, spiral process.

According to Openchowsky, every part of the heart (frog triton, tortoise) contains nerve-fibres which are connected with the muscular fibres. In the auricles, at the end of the non-medullated fibre, a tri-radiate nucleus exists which gives off fibrils to the muscular bundles. There is a network of fine nerve-fibres distributed immediately under the endocardium—these fibres act partly in a centripetal direction on the cardiac ganglia, and are partly motor for the endocardial muscles. The parietal layer of the pericardium contains (sensory) nerve-fibres. The following kinds of nerve-cells are found—*unipolar cells*, the single processes of which afterwards divide; *bipolar pyriform cells* (fig. 66), which in the frog possess a straight (n) and also a spiral process (o) (§ 321).

58. THE AUTOMATIC MOTOR CENTRES OF THE HEART.—(1) It is generally assumed that the nervous centres which excite the cardiac movements,

and maintain the rhythm of these movements, lie within the heart, and that they are probably represented by the *ganglia*. [The heart, however, can execute rhythmical pulsations without the presence of ganglionic structures, p. 95.]

(2) There are—not one, but several of these centres in the heart, which are connected with each other by conducting paths. As long as the heart is intact, all

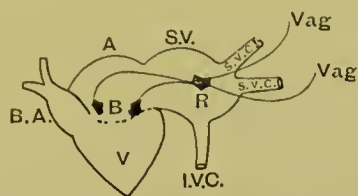


Fig. 67.

Scheme of nerves of frog's heart. R. Remak's, and B, Bidder's ganglia; S.V., sinus venosus; A, auricles; V. ventricle; B.A., bulbus arteriosus; vag, vagi.

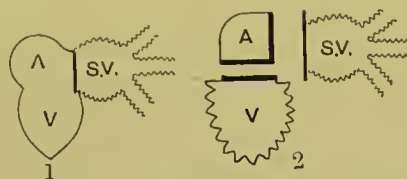


Fig. 68.

Stannius's experiment. A, auricle; V, ventricle; S.V., sinus venosus. The zig-zag lines indicate which parts continue to beat; in 2 the ventricle beats at a different rate.

its parts move in rhythmical sequence from a principal central point, an impulse being conducted from this centre through the conducting paths. What the "discharging forces" of these regular progressive movements are is unknown. If, however, the heart be subjected to the action of diffuse stimuli (*e.g.*, strong electrical currents), all the centres are thrown into action, and a spasm-like action of the heart occurs. The *dominating centre lies in the auricles*, hence the regular progressive movement usually starts from them. If the excitability is diminished, as by touching the septum with opium, other centres seem to undertake this function, in which case the movement may extend from the ventricles to the auricles. According to Kronecker and Schmey, in the *dog's* heart there is a spot above the lower limit of the upper third of the ventricular septum, which, when it is injured, *e.g.*, by destroying it with a stout needle, brings the heart to a standstill; this has been called a co-ordinating centre. [The existence of this centre is denied by some observers.]

(3) All stimuli of moderate strength applied directly to the heart cause at first an increase of the rhythmical heart-beats; stronger stimuli cause a diminution, and it may be paralysis, which is often preceded by a convulsive movement. Increased activity exhausts the energy of the heart sooner.

(4) Single very weak stimuli, which have no effect on the heart when applied singly, if repeated sufficiently often, may become active owing to "summation of the stimuli" (*v. Basch*).

(5) Even the weakest stimulus which can excite a contraction always causes an energetic contraction, *i.e.*, "the minimal stimulus causes a maximal effect" (*Bowditch, Kronecker and Stirling*).

(6) After every contraction of the heart there is a short period of "diminished excitability", or Marey's "refractory period," during which the heart is less susceptible to further stimulation.

(7) The non-ganglionic apex of the heart, when it is not stimulated, no longer beats spontaneously, but it responds each time by a single contraction to a single direct stimulus. If, however, a continuous stimulus, *e.g.*, a continuous current of electricity, be applied to it, it executes a series of beats. Such continuous stimuli are obtained through a continuous pressure of fluid, exerted on the interior of the heart, or by moistening the heart with chemical substances.

(8) The auricular centres seem to be more excitable than those of the ventricle; hence, in a heart left to itself the auricles pulsate longest.

(9) The heart may be excited (reflexly) from its inner surface. Weak stimuli applied to the inner surface of the heart greatly accelerate the heart's action, the stimulus required being much feebler than that applied to the external surface of the heart. Strong stimuli, which bring the heart to rest, also act more easily when applied to its inner surface than when they are applied to its outer surface. The ventricle is always the first part to be paralysed.

(10) In order that the heart may continue to contract, it is necessary that it be supplied with a fluid which, in addition to O, must contain the *necessary nutritive materials*. The most perfect fluid, of course, is blood. Hence the heart after a time ceases to beat in an indifferent fluid (0·6 per cent. sodium chloride), but its activity may be revived by supplying it with a proper nutritive fluid.

Cardiac Nutritive Fluids.—These nutritive fluids are such as contain serum-albumin, *e.g.*, blood, serum, or lymph. Serum retains its nutritive properties even after it has been subjected to diffusion (*Martius and Kronecker*). Milk and whey (*v. Ott*), normal saline solution mixed with blood, albumin, or peptone, and 0·3 per cent. sodium carbonate (*Kronecker, Merunowicz and Stiénon*), a trace of caustic soda (*Gaule*), or a solution of the salts of serum, are suitable. Alkaline solution of soda revives a feebly beating heart by neutralising the acid formed in the cardiac muscle, and so does normal saline containing calcic phosphate and potassic chloride (*S. Ringer*).

(11) The independent pulsations of parts of the heart which are devoid of ganglia show that the presence of ganglia is not absolutely necessary in order to have rhythmical pulsation. Direct stimulation of the heart may cause these movements. But the ganglia are more excitable than the heart muscle itself, and they conduct the impulses which lead to the regular alternating action of the various parts of the heart, so that, under normal circumstances, we must assume that the action of the heart is governed by the ganglia.

(12) If a heart be cut in pieces, so that the individual pieces still remain connected with each other, the regular peristaltic or wave-like movements proceeding from the auricles to the ventricle may continue for a long time (*Donders, Engelmann*). If the heart, however, be completely divided into two distinct pieces (auricle and ventricle), the movements of both parts continue, but not in the same sequence—they beat at different rates.

The chief experiments upon which the above statements are based are as follows:—

I. Experiments by **cutting** and **ligaturing** the heart. These experiments have been made chiefly upon the heart of the frog. The **ligature** experiments are performed by tightening and then relaxing a ligature placed around the heart, so that the physiological connection is destroyed, while the anatomical or mechanical connections (continuity of the cardiac wall, intact condition of its cavities) still exist. The most important of these experiments are—

(1) **Stannius's Experiment.**—If the sinus venosus of a frog's heart be separated from the auricles, either by an incision or by a ligature, the auricles and ventricle stand still in diastole, whilst the veins and the remainder of the sinus continue to beat (fig. 68, 1). If a second incision be made at the auriculo-ventricular groove, as a rule the ventricle begins at once to beat again, whilst the auricles remain in the condition of diastolic rest. [Thus the sinus venosus and ventricle continue to beat, while the auricle stands still, but the two former no longer beat with the same rhythm, the ventricle usually beats more slowly, as is shown in fig. 68, 2, by the large zig-zags.] According to the position of the second ligature or incision, the auricles may also beat along with the ventricles, or the auricles alone may beat while the ventricles remain at rest.

Theoretical.—Various explanations of these experiments have been given:—(A) Remak's ganglion in the sinus venosus is distinguished by its great excitability, while Bidder's ganglion in the auriculo-ventricular groove is less excitable; in the normal condition of the heart the motor impulse is carried from the former to the latter. If the sinus venosus be separated from the heart, Remak's ganglion has no action on the heart. The heart stops for two reasons—

first, because Bidder's ganglion alone has not sufficient energy to excite it to action, and because the inhibitory fibres of the vagus going to the heart have been stimulated by being divided at this point (*Heidenhain*). [That stimulation of the inhibitory fibres of the vagus is not the cause of the standstill is proved by the fact that the standstill occurs even after the administration of atropine, which paralyzes the cardiac inhibitory mechanism.] The passive heart, however, may be made to contract by mechanically stimulating Bidder's ganglion, *e.g.*, by a slight prick with a needle in the auriculo-ventricular groove, or by the action of a constant current of moderate strength (*Eckhard*), the ventricular pulsation at the same time preceding the auricular (*v. Bezold, Bernstein*). If the auriculo-ventricular groove be divided, the ventricle pulsates again, because Bidder's ganglion has been stimulated by the act of dividing it; while, at the same time, the ventricle is withdrawn from the inhibitory influence of the vagus produced by the first division at the sinus venosus. If the line of separation is so made that Bidder's ganglion remains attached to the auricles, these pulsate, and the ventricle rests; if it be divided into halves, the auricles and ventricles pulsate, each half being excited by the portion of the ganglion in relation with it. (B) According to another view, both Renak's (*a*) and Bidder's ganglia (*b*) are motor centres, but in the auricles there is in addition an *inhibitory ganglionic system* (*c*) (*Bezold, Traube*). Under normal circumstances *a + b* is stronger than *c*, while *c* is stronger than *a* or *b* separately. If the sinus venosus be separated it beats in virtue of *a*; on the other hand, the heart rests because *c* is stronger than *b*. If the section be made at the level of the auriculo-ventricular groove, the auricles stand still owing to *c*, while the ventricle beats owing to *b*.

(2) **Descarte's Experiment** (1644).—If the ventricle of a frog's heart be separated from the rest of the heart by means of a **ligature**, or by an **incision** carried through it at the level of the auriculo-ventricular groove, the sinus and atria pulsate undisturbed as before, but the ventricle stands still in diastole. A single local stimulus applied to the ventricle is responded to by a *single* contraction. If the incision be so made that the lower margin of the auricular septum remains attached to the ventricle, the latter pulsates. Even the ventricles of a rabbit's heart, when separated along with a part of the auricles in connection with them, pulsate (*Tigerstedt*).

[**Gaskell's Clamp**.—Gaskell uses a clamp, regulated by a millimetre screw, to compress the heart, and thus to obstruct the passage of impulses from one part of the heart to the other, or to "block" the way, the pulsations of the auricles and ventricles being separately registered. By compressing the heart at the auriculo-ventricular groove, the ratio of auricular and ventricular beats alters, and instead of being 1 : 1, there may be 2, 3, or more auricular beats for each

beat of the ventricle, expressed thus— $\frac{A}{V}, \frac{II}{I}, \frac{III}{I}, \frac{IV}{I}$. After the heart is fixed by the clamp, levers are placed horizontally above and below the heart. These levers are fixed to a part of the auricles and to the apex by means of threads. Each part of the heart attached to a lever, as it contracts, pulls upon its own lever, so that the extent and duration of each contraction may be registered. This method is applicable for studying the effect of the vagus and other nerves upon the heart.]

(3) **Section**.—A. Fick showed that the process of excitement in the contractile tissue of the frog's heart is propagated in all directions (1874), so that to a certain extent the whole frog's heart behaves like *one* continuous muscular fibre; thus one transverse cut into the ventricle does not prevent contraction from taking place in the separated parts. Engelmann's experiments also show that if the ventricle of a frog's heart be cut up into two or more strips in a zig-zag way, so that the individual parts still remain connected with each other by muscular tissue, the strips still beat in a regularly progressive rhythmical manner, provided one strip is caused to contract. The rapidity of the transmission is about 10 to 15 mm. per sec. Hence it appears that the conducting paths for the impulse causing the contraction are not nervous, but must be the contractile mass itself. It has not been proved that nerve-fibres proceed from the ganglia to all the museles.

[According to Marchand's experiments, it takes a very long time for the excitement to pass from the auricles to the ventricle—a much longer time, in fact, than it would require to conduct the excitement through muscle—so that it is probable that the propagation of the impulse from the auricles to the ventricle is conducted by nervous channels to the auriculo-ventricular nervous apparatus. In fact, in the mammalian heart the muscular fibres of the auricles are quite distinct from those of the ventricles.]

(4) When the apex of a frog's heart is ligatured off from the rest of the heart, it no longer pulsates (*Heidenhain, Goltz*), but such an apex, if stimulated directly, *e.g.*, by a prick of a pin, responds with a single contraction. If the "heart-apex" be filled with normal saline solution under pressure, which acts as a stimulus, the heart begins to pulsate, and the same is the case with a solution of delphinin or quinine. If a cannula be tied into the heart over the auriculo-ventricular groove, the ventricle does not beat, but if the ventricle be filled through the cannula with blood containing oxygen, under a constant and sufficient pressure, it pulsates (*Ludwig and Merunowicz*).

[(5) Luciani found that a heart ligatured above the auriculo-ventricular groove, when filled with pure serum, produced *groups of pulsations* with a long diastolic pause between every two groups (fig. 69). The successive beats in each group

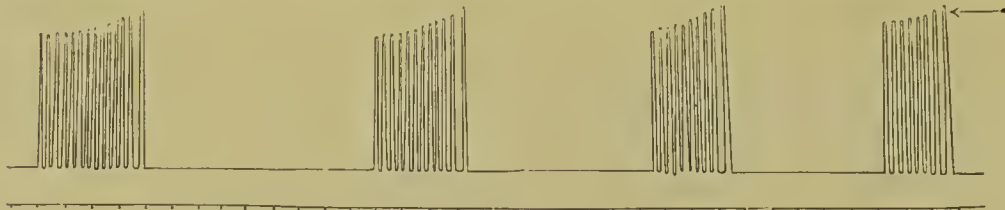


Fig. 69.

Four groups of pulsations with intervening pauses, with their "staircase" character. The points on the abscissa were marked every 10 seconds.

assume a "staircase" character (p. 98). These periodic groups undergo many changes; they occur when the heart is filled with pure serum free from blood-corpuscles, and they disappear and give place to regular pulsations when defibrinated blood or serum containing hæmoglobin or normal saline solution is used (*Rosbach*). They also occur when the blood within the heart has become dark-coloured, *i.e.*, when it has been deprived of certain of its constituents, and if a trace of *veratrin* be added to bright red blood they occur.]

(6) An apex preparation, when stimulated with even a weak induction shock, always gives its maximal contraction, and when a tetanising current is applied tetanus does not occur (*Kronecker and Stirling*). When the opening and closing shocks of a sufficiently strong constant current are applied to the heart-apex, it contracts with each closing or opening shock. [When a *constant* current is applied to the lower two-thirds of the ventricle (heart-apex), under certain conditions the apex contracts *rhythmically*. This is an important fact in connection with any theory of the cardiac beat.]

(7) If the bulbus aortæ (frog) be ligatured, it still pulsates, provided the internal pressure be moderate. Should it cease to beat, a single stimulus makes it respond by a series of contractions. Increase of temperature to 35° C., and raising the pressure within it, increase the number of pulsations (*Engelmann*).

Action of Fluids.—Haller was of opinion that the venous blood was the natural stimulus which caused the heart to contract. That this is not so is proved at once by the fact that the heart beats rhythmically when it contains no blood. Blood and other fluids which are supplied to an excised heart are not the cause of its rhythmical movements, but only the conditions on which these movements depend.

[**Methods.**—The study of the action of fluids upon the excised frog's heart has been rendered possible by the invention of Ludwig's "**frog-manometer**." The apparatus, as modified by Kronecker (fig. 70), consists of (1) a double-way cannula, *c*, which is tied into the heart, *h*; (2) a manometer, *m*, connected with *c*, and registering the movements of its mercury on a revolving cylinder, *cyl*; (3) two Marriotte's flasks, *a* and *b*, which are connected with the other limb of the cannula. Either *a* or *b* can be placed in communication with the interior of the heart by means of the stop-cock, *s*. To the fluid in one graduated tube may be added the substance whose effect on the heart it is proposed to investigate, while the fluid in the other vessel

remains without the addition of any substance and can be used as a control-fluid; *d* is a glass vessel for fluid, in which the heart pulsates, *e'* and *e* are electrodes, *e* is inserted into the fluid in *d*, *e'* is attached to the German silver cannula which is shown in fig. 71.]

[In the tonometer of Roy (figs. 72 and 73) the ventricle, *h*, or the whole heart, is placed in an air-tight chamber, *o*, filled with oil. As before, a "perfusion" cannula is tied into the heart. A piston, *p*, works up and down in a cylinder, and is adjusted by means of a thin flexible animal membrane, such as is used by perfumers. Attached to the piston by means of a thread is a writing-lever, *l*, which records the variations of pressure within the chamber, *o*. When the ventricle contracts, it becomes smaller, diminishes the pressure within *o*, and hence the piston and lever rise; conversely, when the heart dilates, the lever and piston descend. Variations in the volume of the ventricle may be registered without in any way interfering with the flow of fluids through it.]

[Two preparations of the frog's heart have been used—(1) The "heart," in which case the cannula is introduced into the heart through the sinus venosus, and a ligature is tied over it *around the auricle*, i.e., above the auriculo-ventricular groove. Thus the auriculo-ventricular ganglia and other nervous structures remain in the preparation. This was the heart preparation employed by Luciani and Roszbach. (2) In the "heart-apex" or apex preparation, the cannula is introduced as before; but the ligature is tied on it over the ventricle several millimetres *below* the auriculo-ventricular groove, so that this preparation contains none of the auriculo-ventricular ganglia, and, according to the usual statement, this part of the heart is devoid of nerve ganglia. This is the preparation which was used by Bowditch, Kronecker and Stirling, Merunowicz, and others.]

[The first effect of the application of the ligature in both cases is, that both preparations cease to beat, but the "heart" usually resumes its rhythmical contractions within several minutes, while the "heart-apex" does not contract spontaneously until after a much longer time (10 to 90 mins.).]

[If the "heart-apex" be filled with a 0.6 per cent. solution of common salt, the contractions are at first of greater extent, but they afterwards cease, and the preparation passes into a condition of "apparent death," lasting 30–90 mins.; while, if the action of the fluid be prolonged, the heart may not contract at all, even when it is stimulated electrically or mechanically. It may be made, however, to pulsate again, if it be supplied with saline solution containing blood (1 to 10 per cent.). If the ventricle be nipped with wire forceps at the junction of the upper with its middle third, so as to separate the lower two-thirds of the ventricle, physiologically but not anatomically, from the rest of the heart, then the apex will cease to contract, although it is still supplied with the frog's own blood (*Bernstein, Bowditch*). The physiologically isolated apex may be made to beat by clamping the aortic branches so as to prevent blood passing out of the heart, and thus raising the intracardiac pressure. The rate of the beat of the apex is independent of and slower than that of the rest of the heart. This experiment proves that the amount of pressure within the apex-cavity is an important factor in the causation of the spontaneous beats of the apex. If blood-serum, to which a trace of delphinin is added, be transfused or "perfused" through the heart, the heart begins to beat within a minute, continues to beat for several seconds, and then stands still in diastole (*Bowditch*). Quinine and a mixture of atropine and muscarin have a similar action. These experiments show that, *provided no nervous apparatus exists within the heart-apex*, the cause of the varying contraction is to be sought for in the musculature of the heart, and that the stimulus necessary for the systole of the heart's apex may arise within itself. If there is no nervous apparatus of any kind present, then we must assume that the heart-muscle may execute rhythmical movements independently of the presence of any nervous mechanism, although it is usually assumed that the ganglia excite the heart-muscle to pulsate rhythmically. It is by no means definitely

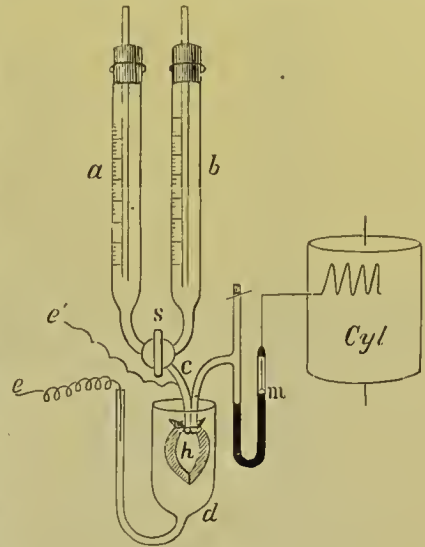


Fig. 70.

Scheme of Kronecker's frog-manometer. *a, b*, Mariotte's flasks for the nutrient fluids; *s*, stop-cock; *c*, cannula; *m*, manometer; *h*, heart; *d*, glass cup for *h*; *e', e*, electrodes; *cyl*, revolving cylinder.

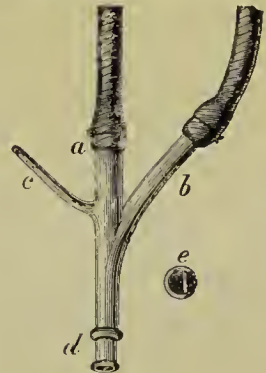


Fig. 71.

Perfusion cannula for a frog's heart. *e*, for fixing an electrode; *d*, the heart is tied over the flanges preventing it from slipping out; *c*, section of *d*.

proved that the heart-apex is devoid of all nervous structures, which may act as originators of these rhythmical impulses.]

[**Action of Drugs.**—If the heart-apex contains no nervous structures, it must form a good object for the study of the action of drugs on the cardiac muscle. Some of these have been mentioned already. Ringer finds that a calcium salt makes the contractions higher and longer. Dilute acids added to saline solution, *e.g.*, lactic, cause complete relaxation of the cardiac musculature, while dilute alkalis produce an opposite effect or tonic contraction, even though the apex be not pulsating. The action of a dilute acid may be set aside by a dilute alkali and *vice versa*. Digitalin, antiarin, barium, and veratria act like alkalis, while saponin, muscarin, and pilocarpin have the effect of acids (§ 65). An isolated frog's heart, fatigued after being supplied with a solution of blood, is caused to beat more vigorously by a solution of kreatinin, or extract of meat (Mays).]

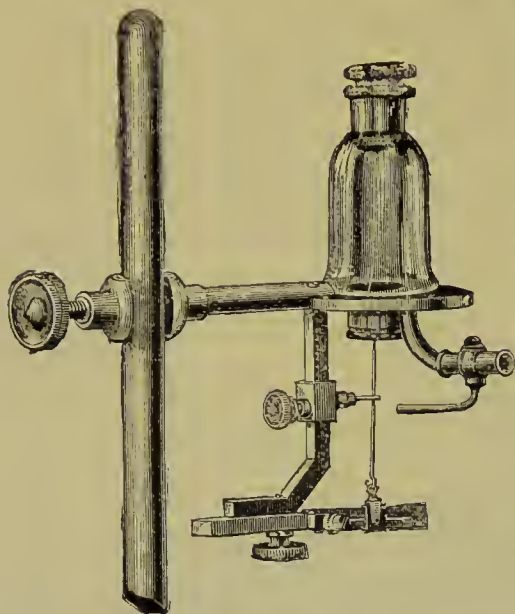


Fig. 72.

Roy's tonometer, as made by the Cambridge Scientific Instrument Company.

(a) **Thermal Stimuli.**—[Heat affects the *number* or *frequency* and the *amplitude* of the pulsations, as well as the *duration* of the systole and diastole and the *excitability* of the heart.] Descartes (1644) observed that heat increased the number of pulsations of an eel's heart. As the temperature increases, the number of beats is at first considerably increased, but afterwards the beats again become fewer, and if the temperature is raised above a certain limit the heart stands still, the myosin of which its fibres consist is coagulated, and "heat-rigor" occurs. Even before this stage is reached, however, the heart may stand still, the muscular fibres appearing to remain contracted. The ventricles usually cease to beat before the auricles (Schelske). The size and extent of the contractions increase up to about 20° C., but above this point they diminish (fig. 74). The time occupied by any single contraction at 20° C. is only about $\frac{1}{15}$ th of the time occupied by a contraction occurring at 5° C. A heart which has been warmed is capable of reacting pretty rapidly to intermittent stimuli, while a heart at a low temperature reacts only to stimuli occurring at a considerable interval (Gauke).

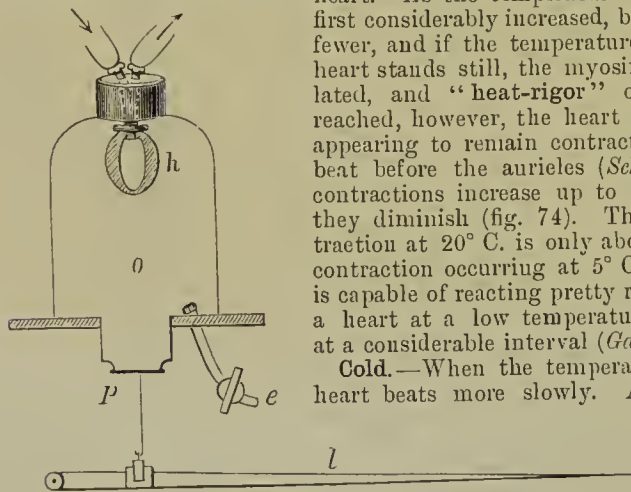


Fig. 73.

Roy's heart tonometer. *h*, heart; *o*, air-tight chamber; *p*, piston; *l*, writing-lever; *e*, outflow tube.

conversely, if it be taken from ice and placed over warm water, it beats more slowly at first and more rapidly afterwards (Aristow).

[**Methods.**—The effect of heat on a heart may be studied by the aid of the frog-manometer, the fluid in which the heart is placed being raised to any temperature required. For demonstration purposes, the heart of a pithed frog is excised and placed on a glass slide under a light

[The "heart" preparation in many respects behaves like the foregoing, *i.e.*, it is exhausted after a time by the continued application of normal saline solution (0.6 per cent. NaCl), while its activity may be restored by supplying it with albuminous and other fluids (p. 92).]

II. Direct Stimulation of the Heart.

—All direct cardiac stimuli act more energetically on the inner than on the outer surface of the heart. If strong stimuli are applied for too long a time, the ventricle is the part first paralysed.

Cold.—When the temperature of the blood is diminished, the heart beats more slowly. A frog's heart, placed between two watch-glasses and laid on ice, beats very much more slowly. The pulsations of a frog's heart stop when the heart is exposed to a temperature of 4° C. to 0°. If a frog's heart be taken out of warm water, and suddenly placed upon ice, it beats more rapidly, and

it beats more slowly at first

lever, such as a straw. The slide is warmed by means of a spirit-lamp. In this way the frequency and amplitude of the contractions are readily made visible at a distance.]

(b) **Mechanical Stimuli.**—Pressure applied to the heart from without accelerates its action. In the case of Fran Serafin, v. Ziemssen found that slight pressure on the auriculo-ventricular groove caused a second short contraction of both ventricles after the heart-beat. Strong pressure causes a very irregular action of the cardiac muscle. This may readily be produced by

compressing the freshly excised heart of a dog between the fingers. The **intra-cardiac pressure** also affects the heart-beat (p. 95). If the pressure within the heart be increased, the heart-beats are gradually increased; if it be diminished, the number of beats diminishes (*Ludwig and Thiry*). If the intra-cardiac pressure be very greatly increased, the heart's action becomes very irregular and slower. A heart which has ceased to beat may under certain circumstances be caused to execute a *single* contraction if it be stimulated mechanically.

(c) **Electrical Stimuli.**—A constant electrical current of moderate strength increases the number of heart-beats. V. Ziemssen found, in the case of Fran Serafin (§ 47, 3), that the number of beats was doubled while a constant uninterrupted strong current was passed through the ventricles. [If the constant current be very strong, or if **tetanising induction currents** be applied to the heart, *e.g.*, of a dog, the normal heart-beat

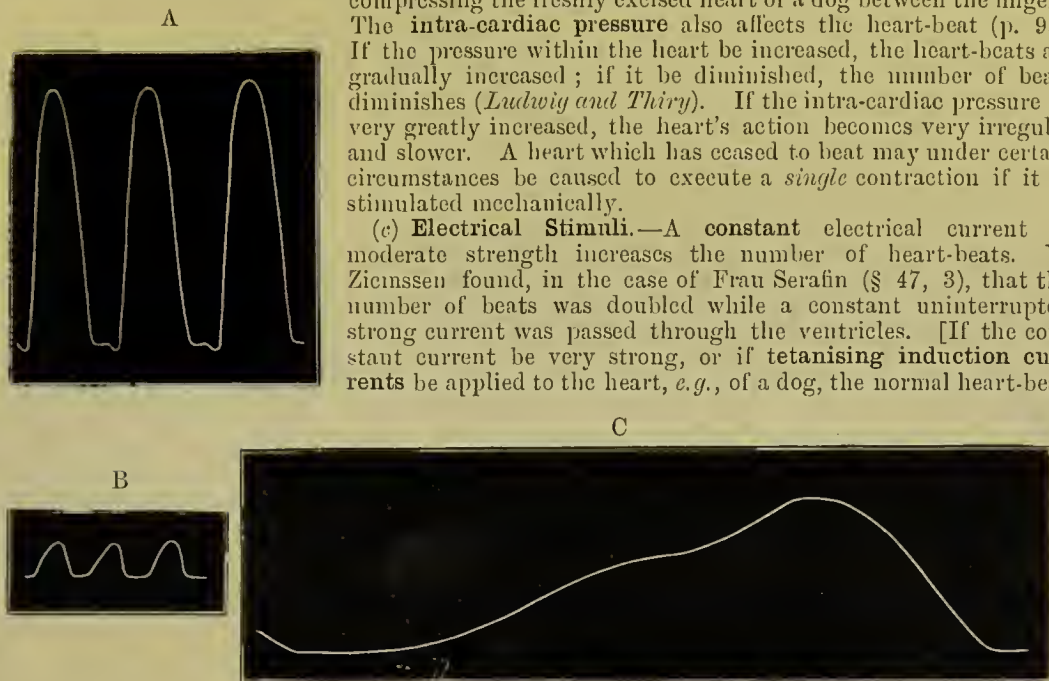


Fig. 74.

A, contraction of a frog's heart at 19° C. ; B, at 34° C. ; C, at 3° C.

is abolished, the ventricular muscle being thrown into a state of irregular, arrhythmic contraction, whilst there is a great fall of blood-pressure (*Ludwig and Hoffa*). This condition is spoken of as **delirium cordis** or **fibrillar contraction**. It is caused by some change in the muscular fibres of the ventricles themselves; the movements are very complex, last long, and occur rapidly; the persistence seems to be due to the great excitability of the ventricular tissue. It appears to consist of a rapid succession of inco-ordinated peristaltic contractions, which may be brought about as described above, or by the action of some depressing agents, *e.g.*, potassic bromide. These ventricular fibrillar contractions are not affected by stimulation of the vagus. Similar electrical stimulation of the auricles causes a fluttering movement, more like a series of contractions, without any distinct sign of inco-ordination. These auricular movements are arrested by stimulation of the vagus (*MacWilliam*).] If the auriculo-ventricular groove be compressed so as to cause the ventricle of a frog's heart to cease to beat, on placing one electrode of a constant current on the ventricular wall and the other electrode on an indifferent part of the body, we obtain, on making the current, a systolic contraction of the ventricle only when the cathode touches the ventricle; and conversely on breaking, only when the anode is on the heart (*Biedermann*).

When a **single induction shock** is applied to the ventricle of a frog's heart during systole, it has no apparent effect; but if it is applied during diastole, the succeeding contraction takes place sooner. The auricles and also the apex behave in a similar manner. Whilst they are contracted, an induction shock has no effect; if, however, the stimulus is applied during diastole, it causes a contraction, which is followed by systole of the ventricle. Even when strong tetanising induction shocks are applied to the heart, they do not produce **tetanus** of the entire cardiac musculature, or, as it is said, "the heart knows no tetanus" (*Kroncker and Stirling*). Small white, local weal-like elevations—such as occur when the intestinal musculature is stimulated—appear between the electrodes. They may last several minutes. A frog's heart, which yields weak and irregular contractions, may be made to execute regular rhythmical contractions synchronous with the stimuli, if electrical stimuli are used (*Bowditch*).

[Break induction shocks, if of sufficient strength, cause the heart to contract, while weak stimuli have no effect; on the other hand, moderate stimuli, when they do cause the heart to contract, always cause a maximal contraction, so that a minimal stimulus acts at the same time

like a maximal stimulus. The heart either contracts, or it does not contract, and when it contracts the result is always a "maximal contraction" (*Kronecker and Stirling*). Bowditch found that the excitability of the heart was increased by its own movements, so that after a heart had once contracted, the strength of the stimulus required to excite the next contraction may be greatly diminished, and yet the stimulus be effectual. Usually the amplitude of the first beat so produced is not so great as the second beat, and the second is less than the third, so that a "staircase" ("Treppe") of beats of successively greater extent was produced (fig. 69). Under certain circumstances, however, a skeletal muscle gives contractions of a "staircase" character. This staircase arrangement occurs even when the strength of the stimulus is kept constant, so that the production of one contraction facilitates the occurrence of the succeeding one. A staircase arrangement of the pulsations is also seen in Luciani's groups (p. 94). The question, whether a stimulus will cause a contraction, depends upon what particular phase the heart is in when the shock is applied. Even comparatively weak stimuli will cause a heart to contract, provided the stimuli are applied at the proper moment and in the proper tempo, *i.e.* to say, they become what are called "infallible." If stimuli are applied to the heart, at intervals which are longer than the time the heart takes to execute its contraction, they are effectual or "adequate," but if they are applied before the period of pulsation comes to an end, then they are ineffectual (*Kronecker*). It is quite clear, therefore, that the relation of the strength of the stimulus to the extent of the contraction of the cardiac muscle is quite different from what occurs in a muscle of the skeleton, where within certain limits the amplitude of the contraction bears a relation to the stimulus, while in the heart the contraction is always *maximal*.]

Human Heart.—V. Ziemssen found that he could not alter the heart-beats of the human heart (*Frau Serafin*, § 47, 3), even with strong induction-currents. The ventricular diastole seemed to be less complete, and there were irregularities in its contraction. By opening and closing, or by reversing a strong *constant* current applied to the heart, the number of beats was increased, and the increase corresponded with the number of electrical stimuli; thus, when the electrical stimuli were 120, 140, 180, the number of heart-beats was the same, the pulse beforehand being 80. The normal pulse-rate of 80 was reduced to 60 and 50 when the number of shocks was reduced in the same ratio. [In Frau Serafin's case the electrodes were applied to the heart, separated from it merely by the pericardium. Ziemssen found that the Faradic current did not modify the heart's action when the thorax was intact, but that the constant current did, if of sufficient strength. Herbst and Dixon Mann obtained negative results with both kinds of electricity in the normal thorax.]

(d) **Chemical Stimuli.**—Many chemical substances, when applied in a dilute solution to the inner surface of the heart, increase the heart-beats, while if they are concentrated, or allowed to act too long, they diminish the heart-beats, and paralyse it. Bile, and bile salts, diminish the heart-beats (also when they are absorbed into the blood as in jaundice); in very dilute solutions both increase the heart-beats. A similar result is produced by acetic, tartaric, citric, and phosphoric acids. Chloroform and ether, applied to the inner surface, rapidly diminish the heart-beats, and then paralyse it; but very small quantities of ether (1 per cent.) accelerate the heart-beat of the frog (*Kronecker and M'Gregor-Robertson*), while a solution of $1\frac{1}{2}$ to 2 per cent. passed through the heart arrests it temporarily or completely. Dilute solutions of opium, strychnia, or alcohol applied to the endocardium increase the heart-beats; if concentrated they rapidly arrest its action. Chloral-hydrate paralyses the heart. [Normal saline (0.6 per cent.) fails to sustain ventricular contractions in the excised batrachian and eel's heart. When the saline is perfused through the heart, in about twenty minutes the heart ceases to beat spontaneously, and is inexcitable to strong induction shocks; but the weakened action may be revived by perfusing normal saline saturated with calcium phosphate and containing a trace of potassium chloride (*Ringer*).]

Action of Gases.—When blood containing different gases was passed through a frog's heart, Klug found that blood containing sulphurous acid rapidly and completely killed the heart; chlorine stimulated the heart at first, and ultimately killed it; and laughing-gas rapidly killed it also. Blood containing sulphuretted hydrogen paralysed the heart without stimulating it. Carbonic oxide also paralysed it, but if fresh blood was transfused the heart recovered. [Blood containing O excites the heart (*Castell*), while the presence of much CO₂ paralyses it, and the presence of CO₂ is more injurious than the want of O. Blood or serum completely saturated with CO₂ exhausts the heart (*Sallet and Kronecker*), but it recovers itself when the CO₂ is removed. H and N have no effect.]

Cardiac Poisons are those substances whose action is characterised by special effects upon the movements of the heart. Amongst these are **neutral potash salts**, which cause the heart to stand still in diastole. [An excised frog's heart ceases to beat after one-half to one minute when it is placed in a 2 per cent. solution of potassic chloride.] Even a very dilute solution of yellow prussiate of potash injected into the heart of a frog causes the ventricle to stand still in systole. **Antiar** (Java arrow-poison) causes the ventricle to stand still in systole and the auricles in diastole. Some heart-poisons, in small doses, diminish the heart's action, and in large doses not unfrequently accelerate it, *e.g.*, digitalis, morphia, nicotin. Others, when given in small doses, accelerate its action, and in large doses slow it—veratria, aconitin, camphor.

Special Actions of Cardiac Poisons.—The complicated actions of various poisons upon the heart have led observers to suppose that there are various intra-cardiac mechanisms on which these substances may act. Besides the *muscular fibres* of the heart and its *automatic ganglia*, some toxicologists assume that there are *inhibitory ganglia* into which the inhibitory fibres of the vagus pass, and *accelerator ganglia*, which are connected with the accelerating nerve-fibres of the heart. *Both the inhibitory and accelerator ganglia are connected with the automatic ganglia by conducting channels.*

Muscarin and all other trimethylammonium bases stimulate permanently the inhibitory ganglia, so that the heart stands still (*Schmiedeberg and Koppe*). According to Gaskell, however, when the action of the sinus is arrested by muscarin, there is no deflection of the galvanometer similar to that produced by the excitation of the vagus. He infers that muscarin does not cause arrest of the beat by acting as an excitant of inhibitory mechanisms, but as a depressant to motor activity.] As atropin and daturin paralyse these ganglia, the standstill of the heart brought about by muscarin may be set aside by atropin. [If a frog's heart be excised and placed in a watch-glass, and a few drops of a very dilute solution of muscarin be placed on it with a pipette, it ceases to beat within a few minutes, and will not beat again. If, however, the muscarin be removed, and a solution of atropin applied to the heart, it will resume its contractions after a short time.] **Physostigmin** or **Calabar bean** excites the energy of the cardiac muscle to such an extent that stimulation of the vagus no longer causes the heart to stand still. **Iodine-aldehyd**, **chloroform**, and **chloral-hydrate** paralyse the automatic ganglia. The heart stands still, and it cannot be made to contract again by atropin. The cardiac muscle itself remains excitable after the action of muscarin and iodine-aldehyd, so that if it be stimulated it contracts. [According to Gaskell, **antiarin** and **digitalin** solutions produce an alteration in the condition of the muscular tissue of the apex of the heart of the same nature as that produced by the action of a very dilute alkali solution, while the action of a blood-solution containing muscarin closely resembles that of a dilute acid solution (p. 110, § 65).]

[**Some Cardiac Poisons**—The cardiac muscle is stimulated, *i.e.*, its contractions become more energetic, the rate of heart-beat remaining the same or becoming slower—under the influence of veratria, digitalin, strophanthus, antiarin, &c., while it is depressed—as shown by diminished energy of contraction, and with final stoppage in diastole—by muscarin, pilocarpin, sapounin, apomorphin, potash salts in large doses, &c. Guanidin, physostigmin, and camphor will cause the heart to beat rhythmically after complete still-stand in diastole by muscarin.]

On the theory that **inhibitory ganglia** are present in the heart, the following drugs—muscarin and physostigmin—by stimulating these ganglia cause arrest of heart's beat in diastole, but the heart still contracts to a mechanical or electrical stimulus. These ganglia are depressed or paralysed by atropin, spartein, duboisin, hyoseyamin, daturin, as shown by the fact that stimulation of the vagus or the sinus venosus no longer arrests the heart's action, nor does the application of muscarin cause any effect.

Nicotin, saponin, and curare depress or paralyse the **vagus-ends in the heart**, as shown by the fact that stimulation of the vagus itself no longer slows or arrests the heart, while muscarin applied to the heart, or stimulation of the sinus venosus, will do so.

Drugs, besides acting directly on the cardiac muscle, or its intra-cardiac nerve-ends and ganglia, may influence the heart in many other ways. One of these is by their action on the **vagus centre** in the medulla oblongata, as shown by the fact that if they stimulate this centre the slowing of the heart-beats thereby produced disappears after the vagi are cut. Amongst drugs acting in this way are digitalis and aconite (after *Boehm and Brunton*).]

[**Nature of a Cardiac Contraction.**—The question as to whether this is a simple contraction or a compound tetanic contraction has been much discussed. So much is certain, that the systolic contraction of the heart is of very much longer duration (8 to 10 times) than the contraction of a skeletal muscle produced by stimulation of its motor nerve. When the sciatic nerve of a nerve-muscle preparation is adjusted upon a contracting heart, a *simple* secondary twitch of the limb, and not a tetanic spasm, is produced when the heart (auricle or ventricle) contracts. This of itself is not sufficient proof that the systole is a simple spasm, for tetanus of a muscle does not in all cases give rise to secondary tetanus in the leg of a rheoscopic limb. Thus, a simple "initial" contraction occurs when the nerve is applied to a muscle tetanised by the action of strychnia, and the contracted diaphragm gives a similar result. The question whether the heart can be tetanised has been answered in the negative, and as yet it has not been shown that the heart can be tetanised in the same way that a skeletal muscle is tetanised.]

[MacWilliam finds, when the quadriceps extensor cruris contracts to cause the knee-jerk, that a sound similar to the first sound of the heart is heard. As the former is regarded as a simple contraction, it is argued that a simple contraction can produce a musculo-sound. Frederique

regards the ventricular systole not as a simple contraction, but as composed of three or more fused contractions corresponding to tetanus. This he concludes from a study of cardiograms as well as from the electro-motive phenomena of the heart.]

The peripheral or extra-cardiac nerves (§§ 369 and 370).

59. CARDIO-PNEUMATIC MOVEMENT.—As the heart within the thorax occupies a smaller space during the systole than during the diastole, it follows that when the glottis is open air must be drawn into the chest when the heart contracts; whenever the heart relaxes, *i.e.*, during diastole, air must be expelled through the open glottis. But we must also take into account the degree to which the larger intra-thoracic vessels are filled with blood. These movements of the air within the lungs, although slight, seem to be of importance in hibernating animals. In animals in this condition the agitation of the gases in the lungs favours the exchange of CO_2 and O in the lungs, and this slow current of air is sufficient to aerate the blood passing through the lungs. [Cecchini called the diminution of the volume of the entire heart which occurs during systole *meiocardia*, and the subsequent increase of volume, when the heart is distended to its maximum, *auxocardia*.]

Method.—A *manometric flame* may be used. Insert one limb of a Y-tube into the opened trachea of an animal, while the other limb passes to a small gas-jet, and connect the other tube with the gas supply. The movements of the heart affect the column of gas, and thus affect the flame. It may also be done in man by inserting the tube into one nostril, while the other nostril and the mouth are closed. [A simpler and less irritating plan is to fill a wide curved glass-tube with tobacco smoke, and insert one end of the tube into one nostril while the other nostril and the mouth are closed. If the glottis be kept open, and respiration be stopped, then the movements of the column of smoke within the tube are obvious. Or a manometer containing a drop of a coloured fluid may be used under the same conditions.]

The *cardiac pneumograph* (fig. 75) consists of a tube (D), about 1 inch in diameter and 6 to 8 inches in length; the tube is bent at a right angle, and communicates with a small metal capsule about the size of a saucer (T), over which a membrane composed of collodion and castor oil is loosely stretched. To this membrane is attached a glass-rod (H) used as a writing-style,

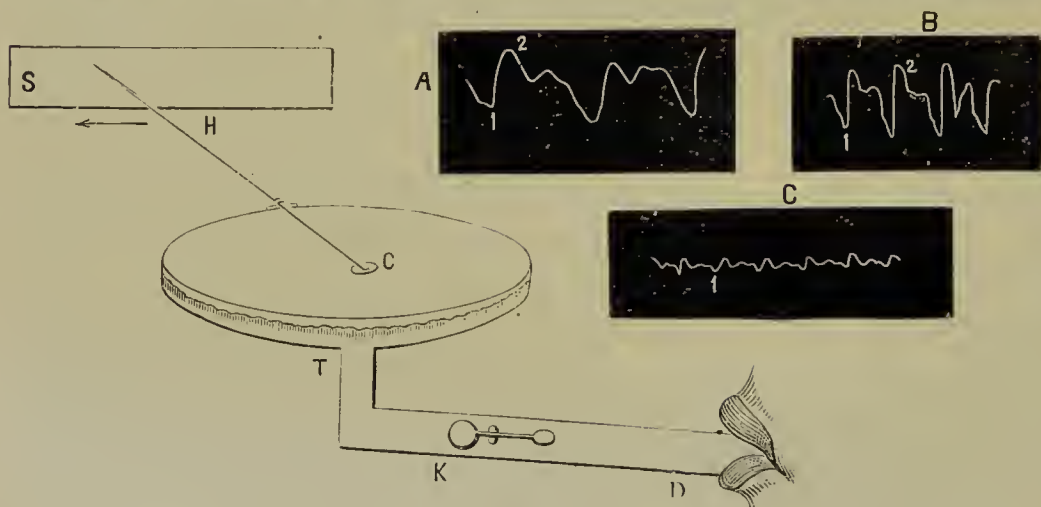


Fig. 75.

Landois' cardio-pneumograph, and the curves obtained therewith. A and B, from man; 1 and 2 correspond to the periods of the first and second heart-sounds; C, from dog; D, method of using the apparatus.

which records its movements on a glass-plate (S) moved by clock-work. A small valve (K) is placed on the side of the tube (D), which enables the experimenter to breathe when necessary. The tube (D) is held in an air-tight manner between the lips, the nostrils being closed, the glottis open, and respiration stopped. In the curves (fig. 75, A, B) we observe that—

(1) At the moment of the first sound (1) the respiratory gases undergo a sharp *expiratory*

movement, because at the moment of the first part of the ventricular systole the blood of the ventricle has not left the thorax, while venous blood is streaming into the right auricle through the venæ cavæ, and because the dilating branches of the pulmonary artery compress the accompanying bronchi. The blood of the right ventricle has not yet left the thorax, it passes merely into the pulmonary circuit. The expiratory movement is diminished somewhat (α) by the muscular mass of the ventricle occupying slightly less bulk during the contraction, and (β) owing to the thoracic cavity being slightly increased by the fifth intercostal space being pushed forward by the cardiac impulse.

(2) Immediately after (1) there follows a strong inspiratory current of the respiratory gases. As soon as the blood from the root of the aorta reaches that part of the aorta lying outside the thorax, more blood leaves the chest than passes into it simultaneously through the venæ cavæ.

(3) After the second sound (at 2), indicated sometimes by a slight depression in the apex of the curve, the arterial blood accumulates, and hence there is another expiratory movement in the curve.

(4) The peripheral wave-movements of the blood from the thorax cause another inspiratory movement of the gases.

(5) More blood flows into the chest through the veins, and the next heart-beat occurs.

60. INFLUENCE OF THE RESPIRATORY PRESSURE ON THE HEART.

The variation in pressure to which all the intra-thoracic organs are subjected, owing to the increase and decrease in the size of the chest caused by the respiratory movements, exerts an influence on the movements of the heart. Examine first the relations in different *passive conditions of the thorax, when the glottis is open*.

The **diastolic dilatation of the cavities of the heart**, besides the pressure of the venous blood and the elastic stretching of the relaxed muscle-wall, is fundamentally due to the **elastic traction of the lungs**. This is stronger the more the lungs are distended (inspiration), and is less active the more the lungs are contracted (expiration). Hence it follows:—

(1) When the greatest possible **expiratory effort** is made (of course, with the glottis open), only a small amount of blood flows into the heart; the heart in diastole is small and contains a small amount of blood. Hence the systole must also be small, thus causing a small pulse-beat.

(2) On taking the greatest possible **inspiration** (with the glottis open), and therefore causing the greatest stretching of the elastic tissue of the lungs, the elastic traction of the lungs is, of course, greatest = 30 mm. Hg, and may interfere with the contraction of the thin-walled atria and appendices, in consequence of which these cavities do not completely empty themselves into the ventricles. The heart is in a state of great diastolic distension, and filled with blood; nevertheless, in consequence of the limited action of the auricles, only small pulse-beats are observed. In several individuals Donders found the pulse to be smaller and slower; afterwards it became larger and faster.

(3) When the chest is in a position of **moderate rest**, whereby the elastic traction is moderate = 7.5 mm. Hg, we have the condition most favourable to the action of the heart—sufficient diastolic dilatation of the cavities of the heart, as well as unhindered emptying of them during systole.

Voluntary increase or diminution of the intra-thoracic pressure affects the action of the heart.

(1) **Valsalva's Experiment (1740).**—If the thorax is fixed in the position of deepest inspiration, and the glottis be then closed, and if a powerful expiratory effort be made by bringing into action all the expiratory muscles, so as to contract the chest, the cavities of the heart are so compressed that the circulation of the blood is temporarily interrupted. In this expiratory phase the elastic traction is very limited, and the air in the lungs being under a high pressure also acts upon the heart and the intra-thoracic great vessels. No blood can pass into the thorax from without; hence the visible veins swell up and become congested, the blood in the lungs is rapidly forced into the left ventricle by the compressed air in the lungs, and the blood soon passed out of the chest, so that the heart and lungs contain little blood, thus leading to a greater supply of blood in the systemic than

in the pulmonary circulation and the heart. The heart-sounds disappear, and the pulse is absent (*E. H. Weber, Donders*).

(2) **J. Müller's Experiment** (1838).—Conversely, if after the deepest possible expiration the glottis be closed, and the chest be now dilated with a great inspiratory effort, the heart is powerfully dilated, the elastic traction of the lungs, and the very attenuated air in these organs, act so as to dilate the cavities of the heart. More blood flows into the right heart, and, in proportion as the right auricle and ventricle can overcome the traction outwards, the blood-vessels of the lungs become filled with blood, and thus partly occupy the lung-space. Much less blood is driven out of the left heart, so that the pulse may disappear. Hence the heart is distended with blood and the lungs are congested, while the aortic system

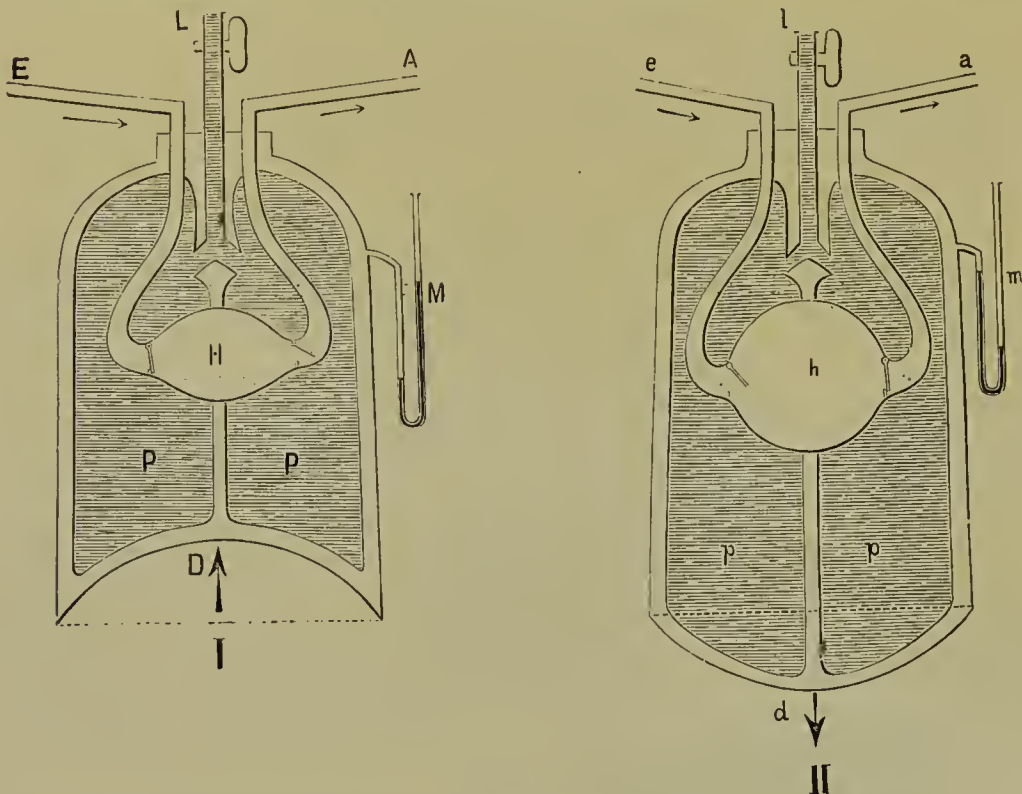


Fig. 76.

Apparatus for demonstrating the action of expiration (I.), and inspiration (II.), on the heart and blood-stream. P, p, lungs; H, h, heart; L, l, closed glottis; M, m, manometers; E, e, ingoing blood-stream, vein; A, a, outgoing blood-stream, artery; D, diaphragm during expiration; d, during inspiration.

contains a small amount of blood, *i.e.*, the systemic circulation is comparatively empty, while the heart and the pulmonary vessels are engorged with blood.

In normal respiration, the air in the lungs during inspiration is under slight pressure, while during expiration the pressure is higher, so that these conditions favour the circulation; inspiration favours the occurrence of diastole, the supply of blood (and lymph) through the *venæ cavæ*. In operations where the axillary or jugular vein is cut, air may be sucked into the circulation during inspiration, and cause death. Expiration favours the flow of blood in the aorta and its branches, and aids the systolic emptying of the heart.

The elastic traction of the lungs aids the **lesser circulation** through the lungs; the blood of the pulmonary capillaries is exposed to the pressure of the air in the lungs, while the blood in the pulmonary veins is exposed to a less pressure, as the

elastic traction of the lungs, by dilating the left auricle, favours the outflow from the capillaries into the left auricle. The elastic traction of the lungs acts slightly as a disturbing agent on the right ventricle, and therefore, on the movement of blood through the pulmonary artery, owing to the overpowering force of the blood-stream through the pulmonary artery, as against the elastic traction of the lungs (*Donders*).

The above apparatus (fig. 76) shows the effect of the inspiratory and expiratory movements on the dilatation of the heart, and on the blood-stream in the large blood-vessels. The large glass vessel represents the thorax; the elastic membrano, D, the diaphragm; P, *p*, the lungs; L, the trachea supplied with a stop-cock to represent the glottis; H, the heart; E, the venæ cavae; A, the aorta. If the glottis be *closed*, and the expiratory phase imitated by pushing up D as in I., the air in P, P and the heart H are compressed, the venous valve closes, the arterial is opened, and the fluid is driven out through A. The manometer, M, indicates the intra-thoracic pressure. If the glottis be closed, and the inspiratory phase imitated, as in II., *p*, *p*, and *h* are dilated, the venous valve opens, the arterial valve closes; hence, venous blood flows from *e* into the heart. Thus, inspiration always favours the venous stream, and hinders the arterial; while expiration hinders the venous, and favours the arterial stream. If the glottis L and *l* be open, the air in P, P, *p*, *p*, will be changed during the respiratory movements D and *d*, so that the action on the heart and blood-vessels will be diminished, but it will still persist, although to a much less extent.

The Circulation of the Blood.

61. FLOW OF FLUIDS THROUGH TUBES.—**Toricelli's Theorem** states that the velocity of efflux (*v*) of a fluid—through an opening at the bottom of a cylindrical vessel—is exactly the same as the velocity which a body falling freely would acquire, were it to fall from the surface of the fluid to the base of the orifice of the outflow. If *h* be the height of the propelling force, the velocity of efflux is given by the formula—

$$v = \sqrt{2gh} \text{ (where } g = 9.8 \text{ metres).}$$

The rapidity of outflow increases with increase in the height of the propelling force, *h*. The former occurs in the ratio 1, 2, 3, when *h* increases in the ratio 1, 4, 9, *i.e.*, the velocity of efflux is as the square root of the height of the propelling force. Hence it follows that the velocity of efflux depends upon the height of the liquid above the orifice of outflow, and not upon the nature of the fluid.

Resistance.—Toricelli's theorem, however, is only valid when all resistance to the outflow is absent; but in every physical experiment such resistance exists. Hence, the propelling force, *h*, has not only to cause the *efflux* of the fluid, but has also to *overcome resistance*. These two forces may be expressed by the heights of two columns of water placed over each other, *viz.*, by the height of the column of water causing the outflow, F, and the height of the column, D, which overcomes the resistance opposed to the outflow of the fluid. So that

$$h = F + D.$$

62. VELOCITY OF THE CURRENT. RESISTANCE.—In the case of a fluid flowing through a tube, which it fills completely, we have to consider the propelling force, *h*, causing the fluid to flow through the various sections of the tube. The amount of the propelling force depends upon two factors:—

(1) On the *velocity of the current*, *v*; (2) on the *pressure* (amount of *resistance*) to which the fluid is subjected at the various parts of the tube, D.

(1) The *velocity of the current*, *v*, is estimated—(a) from the lumen, *l*, of the tube; and (b) from the quantity of fluid, *q*, which flows through the tube in the unit of time. So that $v = q : l$. Both values, *q* as well as *l*, can be accurately measured. (The circumference of a circular tube,

whose diameter = *d* is $3.14 d$. The sectional area (lumen of the tube) is $l = \frac{3.14}{4} d^2$). Having in

this way determined *v*, from it we may calculate the height of the column of fluid, F, which will give this velocity, *i.e.*, the height from which a body must fall in vacuo, in order to attain the velocity *v*. In this case $F = \frac{v^2}{4g}$ where *g* = the distance traversed by a falling body in 1 sec.

= 4.9 metres).

(2) The *pressure*, D (amount of resistance), is measured directly by placing manometers at different parts of the tube (fig. 78).

The propelling force at any part of the tube is—

$$h = F + D$$

$$\text{or } h = \frac{v^2}{4g} + D \text{ (Donders).}$$

This is proved experimentally by taking a tall cylindrical vessel, A, of sufficient size, which is kept filled with water at a constant level, h . The rigid outflow tube, ab , has in connection with it a number of tubes placed vertically, 1, 2, 3, constituting a piezometer. At the end of the

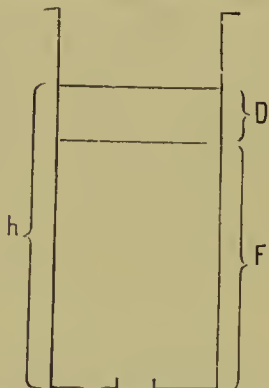


Fig. 77.

Cylindrical vessel filled with water.
 h , height of the column of fluid;
 D , height required to overcome the resistance; F , height causing the efflux.

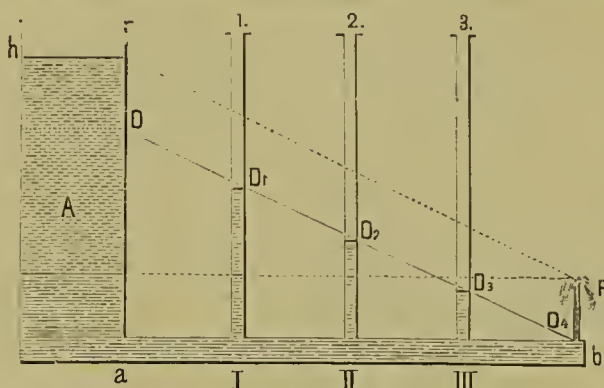


Fig. 78.

A, cylindrical vessel filled with water; ab , outflow tube, along which are placed at intervals vertical tubes, 1, 2, 3, to estimate the pressure.

tube, b , there is an opening with a short tube fixed in it, from which the water issues to a constant height, provided the level of h is kept constant. The height to which it rises depends on the height of the column of fluid causing the velocity, F . As the pressure in the manometric tubes, D^1 , D^2 , D^3 , can be read off directly, the propelling force of the water at the sections of the tubes, I, II, III, is—

$$h = F + D^1; F + D^2; F + D^3.$$

At the end of the tube, b , where $D^4 = 0$, $h = F + 0$, *i.e.*, $h = F$. In the cylinder itself it is the constant pressure, h , which causes the movement of the fluid. It is clear that the propelling force of the water gradually diminishes as we pass from the inflow towards the outflow of the tube, b . The water in the pressure-cylinder, falling from the height, h , only rises as high as F at b . This diminution of the propelling power is due to the presence of **resistances**, which oppose the current in the tube, *i.e.*, part of the energy is transformed into heat. As the propelling force at b is represented only by F , while in the vessel it is h , the difference must be due to the sum of the resistances, $D = h - F$; hence it follows that $h = F + D$.

Estimation of the Resistance.—When a fluid flows through a tube of uniform calibre, the propelling force, h , diminishes from point to point on account of the uniformly acting resistance, hence the sum of the resistance in the whole tube is directly proportional to its length. In a uniformly wide tube, fluid flows through each sectional area with equal velocity, hence v and also F are equal in all parts of the tube. The diminution which h (propelling force) undergoes can only occur from a diminution of pressure D , as F remains the same throughout (and $h = F + D$). Experiment with the pressure-cylinder shows that the pressure towards the outflow end of the tube gradually diminishes. *In a uniformly wide tube, the height of the pressure in the manometers expresses the resistances opposed to the current of fluid which it has to overcome in its course from the point investigated to the free orifice of efflux.*

Nature of the Resistance.—The resistance opposed to the flow of a fluid depends upon the *cohesion of the particles* of the fluid amongst themselves. During the current, the outer layer of fluid which is next the wall of the tube, and which moistens it, is at rest. All the other layers of fluid, which may be represented as so many cylindrical layers, one inside the other, move more rapidly as we proceed towards the axis of the tube, the axial thread or stream being the most rapidly moving part of the liquid. On account of the movement of the cylindrical layers, one within the other, a part of the propelling energy must be used up. The amount of the resistance greatly depends upon the *amount of the cohesive force* which the particles of the fluid have for each other; the more firmly the particles cohere the greater will be the resistance, and *vice versâ*. Hence, the sticky blood-current experiences greater resistance than water or ether.

Heat diminishes the cohesion of the particles, hence it also diminishes the resistance to the outflow. These resistances are first developed by, and result from, the movement of the particles of the fluid, they being, as it were, torn from each other. *The more rapid the current, therefore, i.e., the larger the number of particles of fluid which are pulled asunder in the unit of time, the greater will be the sum of the resistance.* As the layer of fluid lying next the tubes, and moistening it, is at rest, the material which composes the tube exerts no influence on the resistance.

Tubes of Unequal Diameter.—When the velocity of the current is uniform, the resistance depends upon the diameter of the tube—the smaller the diameter the greater the resistance, the greater the diameter the less the resistance. The resistance in narrow tubes, however, increases more rapidly than the diameter of the tube decreases, as has been proved experimentally. In tubes of unequal calibre, at different parts of their course, the velocity of the current varies—it is slower in the wide part of the tube and more rapid in the narrow parts. As a general rule, in tubes of unequal diameter the velocity of the current is inversely proportional to the diameter of the corresponding section of the tube; *i.e.*, if the tube be cylindrical, it is inversely proportional to the square of the diameter of the circular transverse section. In tubes of uniform diameter, the propelling force of the moving fluid diminishes *uniformly* from point to point, but in tubes of *unequal* calibre it does *not* diminish *uniformly*. As the resistance is greater in narrow tubes, of course the propelling force must diminish more rapidly in them than in wide tubes. Hence, within the wide parts of the tube the pressure is greater than the sum of the resistances still to be overcome, while in the narrow portions it is less than these.

Tortuosities and bending of the vessels add new resistance, and the fluid presses more strongly on the convex side than on the concave side of the bend, and there the resistance to the flow is greater than on the concave side.

Division of a tube into two or more branches is a source of resistance, and diminishes the propelling power. When a tube divides into two smaller tubes, of course some of the particles of the fluid are retarded, while others are accelerated on account of the unequal velocities of the different layers of the fluid. Many particles which had the greatest velocity in the axial layer come to lie more towards the side of the tube where they move more slowly; and conversely many of those lying in the outer layers reach the centre, where they move more rapidly. Hence, some of the propelling force is used up in this process, and the pulling asunder of the particles where the tube divides acts in a similar manner. If two tubes *join* to form *one* tube, new resistance is thereby caused, which must diminish the propelling force. The sum of the mean velocities in both branches is independent of the *angle* at which the division takes place (*Jacobson*). If a branch be opened from a tube, the principal current is accelerated to a considerable extent, no matter at what angle the branch may be given off.

63. FLOW IN CAPILLARY TUBES.—Poiseuille proved experimentally that the flow in the capillaries is subject to special conditions—

(1) The quantity of fluid which flows out of the *same* capillary tube is proportional to the pressure.

(2) The time necessary for a given quantity of fluid to flow out (with the like pressure, diameter of tube and temperature), is proportional to the length of the tubes.

(3) The product of the outflow (other things being equal) is as the fourth power of the diameter.

(4) The velocity of the current is proportional to the pressure and to the square of the diameter, and inversely proportional to the length of the tube.

(5) The resistance in the capillaries is proportional to the velocity of the current.

64. FLOW IN ELASTIC TUBES.—(1) When an uninterrupted *uniform* current flows through an elastic tube, it follows exactly the *same laws* as if the tube had *rigid walls*. If the propelling power increases or diminishes, the elastic tubes become wider or narrower, and they behave, as far as the movement of the fluid is concerned, as wider or narrower rigid tubes. Hamel has shown that elastic tubes transmit more fluid when they undergo a rhythmical pulsatory movement than when the fluid flows into them under constant pressure. The advantage of rhythmical impulses for the onward flow in relation to a fluid in motion, as compared with a continuous uniform pressure, seems to be due to the alternate movement keeping the elasticity of the arterial walls intact.

(2) **Wave-Motion.**—If, however, more fluid be forced *in jerks* into an elastic tube, *i.e.*, *interruptedly*, the first part of the tube dilates suddenly, corresponding to the quantity of fluid propelled into it. The jerk communicates an *oscillatory* movement to the particles of the fluid, which is communicated to all the fluid particles from the beginning to the end of the tube; *a positive wave is thus rapidly propagated throughout the whole length of the tube.* If we imagine the elastic tube to be closed at its peripheral end, the positive wave will be reflected from the point of occlusion, and it may be propagated to and fro through the tube until it finally disappears. In such a closed tube a sudden jet of fluid produces only a *wave-movement*, *i.e.*, only a vibratory movement, or an alteration in the shape of the liquid, there being no actual translation of the particles along the tube.

(3) If, however, fluid be pumped interruptedly or by jerks into an elastic tube filled with fluid, in which there is already a continuous current, the movement of the current is combined with the wave movement. We must carefully distinguish the *movement of the current of the fluid*, i.e., the translation of a mass of fluid through the tube, from the *wave-movement*, the oscillatory movement, or movement of change of form in the column of fluid. In the former the particles are actually translated, while in the latter they merely vibrate. The current in elastic tubes is slower than the wave-movement, which is propagated with great rapidity. This last case obtains in the arterial system. The blood in the arterics is already in a state of continual movement, directed from the aorta to the capillaries; by means of the systole of the left ventricle a quantity of fluid is suddenly pumped into the aorta, and causes a *positive wave*, the *pulse-wave* which is propagated with great rapidity to the terminations of the arteries, while the current of the blood itself moves much more slowly.

Rigid and Elastic Tubes.—If a quantity of fluid be forced into a *rigid tube* under a certain pressure, the same quantity of fluid will flow out at once at the other end of the tube, provided there be no special resistance. In an *elastic tube*, immediately after the forcing in of a quantity of fluid, at first only a small quantity flows out, and the remainder flows out only after the propelling force has ceased to act. If an equal quantity of fluid be *periodically* injected into a *rigid tube*, with each jerk an equal quantity is forced out at the other end of the tube, and the outflow lasts exactly as long as the jerk or the contraction, and the pause between two periods of outflow is exactly the same as between the two jerks or contractions. In an *elastic tube* it is different, as the outflow continues for a time after the jerk; hence it follows that a continuous outflow current will be produced in elastic tubes, when the time between two jerks is made shorter than the duration of the outflow after the jerk has been completed. When fluid is pumped periodically into rigid tubes, it causes a sharp abrupt outflow synchronous with the inflow, and the outflow becomes continuous only when the inflow is continuous and uninterrupted. In elastic tubes, an intermittent current under the above conditions causes a continuous outflow, which is increased with the systole or contraction.

65. STRUCTURE AND PROPERTIES OF THE BLOOD-VESSELS.—In the body the large vessels carry the blood to and from the various tissues and organs, while the thin-walled capillaries bring the blood into intimate relation with the tissues. Through the excessively thin walls of the capillaries the fluid part of the blood transudes, to nourish the tissues outside the capillaries, so that the capillary wall is permeable to fluids and gases, and, we shall see, also to the red and white corpuscles of the blood. [At the same time fluids pass from the tissues into the blood. Thus, there is an exchange between the blood and the fluids of the tissues. The fluid after it passes into the tissues constitutes the **lymph**, and acts like a stream *irrigating* the tissue elements.]

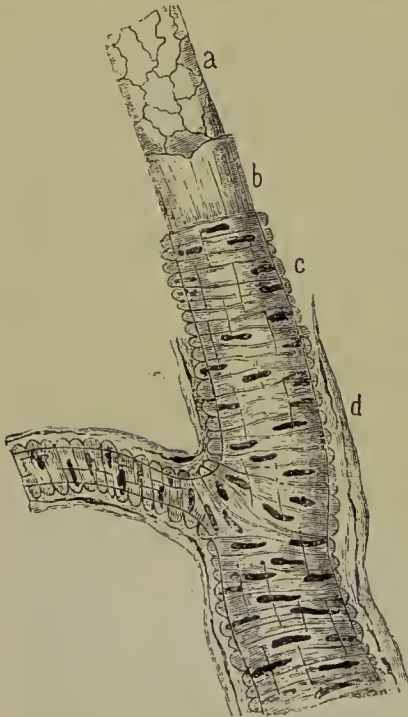


Fig. 79.

Coats of a small artery. *a*, endothelium; *b*, internal elastic lamina; *c*, circular muscular fibres of the middle coat; *d*, the outer coat.

I. The arteries are distinguished from veins by their *thicker walls*, due to the greater development of smooth muscular and elastic tissues—the middle coat (tunica media) of the arteries is specially thick, while the outer coat (t. adventitia) is relatively thin. [When cut across, the walls do not collapse, as is the case with the thin-walled veins. The absence of valves is by no means a characteristic feature.]

A typical artery consists of three coats (figs. 79, 80). (1) The *tunica intima*, or inner coat, consists of a layer of (*a*) irregular, long, fusiform, nucleated, squamous cells forming the excessively thin transparent **endothelium** immediately in contact with the blood-stream. [Like other endothelial cells, these cells are held together by a cement substance, which is blackened by the action of silver nitrate and subsequent exposure to light.] Outside this

lies a very thin, more or less fibrous, layer—**sub-epithelial layer**—in which numerous spindle or

branched protoplasmic cells lie embedded within a corresponding system of plasma canals. Outside this is an **elastic lamina** (*b*), basement membrane, or *membrana propria*, which in the *smallest arteries* is a structureless or fibrous elastic membrane—in arteries of *medium size* it is a fenestrated membrane (*Henle*), while in the *largest arteries* there may be several layers of elastic laminae or fenestrated elastic membrane mixed with connective tissue. [In some arteries the elastic membrane is distinctly fibrous, the fibres being chiefly arranged longitudinally. It can be stripped off, when it forms a brittle elastic membrane, which has a great tendency to curl up at its margins. In a transverse section of a middle-sized empty artery it appears as a bright wavy line, but the curves are produced by the partial collapse of the vessel. It forms an important guide to the pathologist, in enabling him to determine which coat of the artery is diseased.] In middle-sized and large arteries a few non-striped muscular fibres are disposed *longitudinally* between the elastic plates or laminae. Along with the circular muscular fibres of the middle coat, they may act so as to narrow the artery, and they may also aid in keeping the lumen of the vessel open and of uniform calibre.

(2) The **tunica media**, or middle coat, contains much non-striped muscle (*e*), which in the *smallest arteries*, sometimes called *arterioles*, consists of transversely disposed non-striped

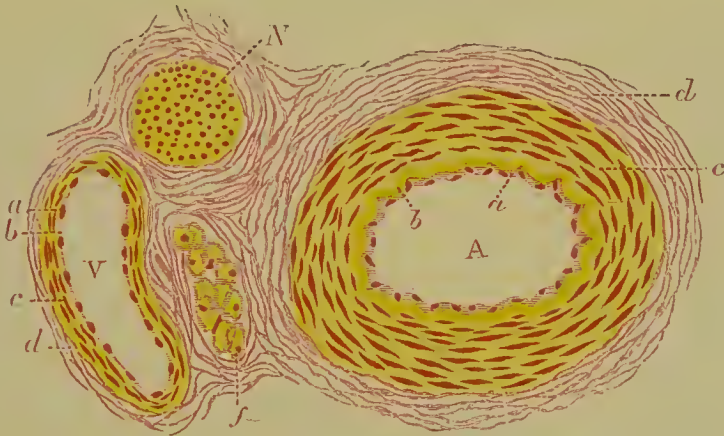


Fig. 80.

Transverse section of a small artery, vein, and nerve. A, artery; *a*, its endothelium; *b*, elastic lamina; *c*, muscular coat, with its rod-shaped nuclei; *d*, adventitia. V, vein; *a*, its endothelium; *b*, thin elastic lamina; *c*, thin muscular coat; *d*, adventitia; *f*, fat. N, transverse section of a nerve.

muscular fibres lying between the endothelium and the T. adventitia, while a finely granular tissue with few elastic fibres forms the bond of union between them. As we proceed from the very smallest to the small arteries, the number of muscular fibres become so great as to form a well-marked fibrous tube of **non-striped muscle**, in which there is comparatively little connective-tissue. In the *large* arteries the amount of connective-tissue is considerably increased, and between the layers of fine connective-tissue numerous (as many as 50) thick, elastic fibrous or fenestrated laminae are concentrically arranged. A few non-striped fibres lie scattered amongst these, and some of them are arranged transversely, while a few have an oblique or longitudinal direction.

The first part of the aorta and pulmonary artery, and the retinal arteries, are devoid of muscle. The descending aorta, common iliac, and popliteal have longitudinal fibres between the transverse ones. Longitudinal bundles lying inside the media occur in the renal, splenic, and internal spermatic arteries. Longitudinal bundles occur both on the outer and inner surfaces of the umbilical arteries, which are very muscular.

(3) The **tunica adventitia**, or outer coat, in the *smallest* arteries consists of a structureless membrane with a few connective-tissue corpuscles attached to it; in *somewhat larger* arteries there is a layer of fine fibrous elastic tissue mixed with bundles of fibrillar connective-tissue (*d*). In arteries of *middle-size*, and in the *largest* arteries, the chief mass consists of bundles of fibrillar connective-tissue containing connective-tissue corpuscles. The bundles cross each other in a variety of directions, and fat cells often lie between them. Next the media there are numerous fibrous or fenestrated elastic lamellae. In medium-sized and small arteries the elastic tissue next the media takes the form of an independent elastic membrane (*Henle's external elastic membrane*). Bundles of non-striped muscle, arranged longitudinally, occur in the adventitia of the arteries of the penis, and in the renal, splenic, spermatic, iliac, hypogastric, and superior mesenteric arteries.

[The following tabular statement may facilitate the study of the arterial coats.

Medium Artery.

TUNICA INTIMA (Inner coat).	{ (a) Endothelium. (b) Sub-endothelial layer. (c) Elastic lamina.
TUNICA MEDIA (Middle coat).	{ Composed of layers of smooth muscular fibres disposed circularly, and scattered amongst these there are sometimes elastic fibres.
TUNICA ADVENTITIA (Outer coat).	{ Composed of connective-tissue, <i>i.e.</i> , white fibrous tissue mixed with elastic fibres, the latter more abundant at the inner part of the coat.]

II. The capillaries (fig. 81), while retaining their diameter, divide and reunite so as to form networks, whose shape and arrangement differ considerably in different tissues. As to their size, the diameter of the capillaries varies considerably, but as a general rule it is such as to admit freely a single row of blood-corpuscles. In the retina and the muscles the diameter is 5-6 μ and in bone-marrow, liver, and choroid 10-20 μ . [In the lungs the capillaries are rather wider than elsewhere.] The tubes consist of a



Fig. 81.

Capillaries. The outlines of the unciliated endothelial cells with the cement blackened by the action of silver nitrate.

a single layer of transparent, excessively thin, nucleated endothelial cells joined to each other by their margins. [Each cell consists of a flattened nucleated plate, for the most part converted into a transparent material. In capillaries the nuclei project slightly and alternately into the lumen of the vessel. The nuclei contain a well-marked intra-nuclear plexus of fibrils, like other nuclei.] The cells are more fusiform in the smaller capillaries and more polygonal in the larger. The body of the cells presents the characters of very faintly refractive protoplasm, but it is doubtful whether the body of the cell is endowed with the property of contractility (p. 110).

If a dilute solution ($\frac{1}{4}$ per cent.) of silver nitrate be injected into the blood-vessels, the cement substance of the endothelium [and of the muscular fibres as well] is revealed by the presence of the black "silver lines." The blackened cement substance shows little specks and large black slits at different points. It is not certain whether these are actual holes through which colourless corpuscles may

pass out of the vessels, or are merely larger accumulations of the cement-substance. [If a capillary is examined in a perfectly fresh condition (while living) and without the addition of any reagent, it is impossible to make out any line of demarcation between adjacent cells owing to the uniform refractive index of the entire wall of the tube.]

[Arnold called these small areas in the black silver lines when they are large *stomata*, and when small *stigmata*. They are most numerous after venous congestion, and after the disturbances which follow inflammation of a part. They are not always present. The existence of cement-substance between the cells may also be inferred from the fact that indigo-sulphate of soda is deposited in it (*Thoma*), and particles of cinnabar and China ink are fixed in it, when these substances are injected into the blood (*Foa*).]

Fine anastomosing fibrils derived from non-medullated nerves terminate in small end-buds in relation with the capillary wall; ganglia in connection with the nerves of capillaries occur only in the region of the sympathetic.

The small vessels next in size to the capillaries, and continuous with them, have a completely structureless covering in addition to the endothelium.

III. The **veins** are generally distinguished from the arteries by their *lumen* being *wider* than the lumen of the corresponding arteries; their *walls are thinner* on account of the smaller amount of non-striped muscle and elastic tissue (the non-striped muscle is not unfrequently arranged longitudinally in veins). [The walls contain relatively much more white fibrous and less elastic tissue.] They are also more *extensile* (with the same strain). The adventitia is usually the thickest coat. The occurrence of **valves** is limited to the veins of certain areas (fig. 82, A). [When empty and cut across, their walls collapse.]

Structure.—(1) The **Tunica intima** consists of a layer of *shorter and broader endothelial cells*, under which in the smallest veins there is a structureless elastic membrane, **sub-epithelial layer**, which is fibrous in veins somewhat larger in size, but in all cases is thinner than in the arteries. [It can scarcely be called a lamina. It is rather an elastic basis, composed of a felted net-work of elastic and white fibres.] In large veins it may assume the characters of a fenestrated membrane, which is double in some parts of the crural and iliac veins. Isolated muscular fibres exist in the intima of the femoral and popliteal veins.

(2) The **T. media** of the larger veins consists of alternate layers of elastic and muscular tissue united to each other by a considerable amount of connective-tissue, but this coat is always thinner than in the corresponding arteries. This coat diminishes in the following order in the following vessels:—popliteal, veins of the lower extremity, veins of the upper extremity, superior mesenteric, other abdominal veins, hepatic, pulmonary, and coronary veins. The following veins contain no muscle:—veins of bone, central nervous system and its membranes, retina, the superior cava, with the large trunks that open into it, the upper part of the inferior cava. Of course, in these cases the media is very thin. In the smallest veins the media is formed of fine connective-tissue, with very few muscular fibres scattered in the inner part.

(3) The **T. adventitia** is thicker than that of the corresponding arteries; it contains *much connective-tissue*, usually arranged longitudinally, and not much elastic tissue. Longitudinally arranged *muscular fibres* occur in some veins (renal, portal, inferior cava near the liver, veins of the lower extremities). The **valves** consist of fine fibrillar connective-tissue with branched cells. An elastic network exists on their convex surface, and both surfaces are covered by endothelium. The valves contain many muscular fibres (fig. 82). [Ranvier has shown that the shape of the epithelial cells on the side over which the blood passes are more elongated than on the cardiac side of the valve, where the long axes of the cells are placed transversely.]

The **sinuses** of the dura mater are spaces covered with endothelium. The spaces are either duplicatures of the membrane, or channels in the substance of the tissue itself.

Cavernous spaces we may imagine to arise by numerous divisions and anastomoses of tolerably large veins of unequal calibre. The vascular wall appears to be much perforated and like a sponge, the internal space being traversed by threads and strands of tissue, which are covered with endothelium on their surfaces, that are in contact with the blood. The surrounding wall consists of connective-tissue, which is often very tough, as in the corpus cavernosum, and it not unfrequently contains non-striped muscle.

Cavernous formations of an analogous nature on *arteries* are the carotid gland of the frog, and a similar structure on the pulmonary arteries and aorta of the turtle, and the coccygeal gland of man. The last structure is richly supplied with sympathetic nerve-fibres, and is a convoluted



Fig. 82.

A, valves in the saphena vein. B, Longitudinal section of a vein at the level of a valve. *a*, hyaline layer of the internal coat; *b*, elastic lamina; *c*, groups of smooth muscular fibres divided transversely; *d*, longitudinal muscular fibres in the adventitia.

mass of anpuUated or fusiform dilatations of the middle sacral artery, surrounded and permeated by non-striped muscle.

Vasa Vasorum.—[These are small vessels which nourish the coats of the arteries and veins. They arise from one part of a vessel and enter the walls of the same, or another vessel at a lower level. They break up chiefly in the outer coat, and none enter the inner coat.] In structure they resemble other small blood-vessels. The blood circulating in the arterial or venous wall is returned by small veins.

[Lymphatics.]—There are no lymphatics on the inner surface of the muscular coat, or under the intima in large arteries. They are numerous in a gelatinous layer immediately outside the muscular coat, and the same relation obtains in large muscular veins and lymphatic trunks (*Hoggan*.)

Intercellular Blood-Channels.—Intercellular blood-channels of narrow calibre, and without walls, occur in the granulation tissue of healing wounds. At first blood-plasma alone is found between the formative cells, but afterwards the blood-current forces blood-corpuscles through the channels. The first blood-vessels in the developing chick are formed in a similar way from the formative cells of the mesoblast.

Properties of the Blood-Vessels.—The larger blood-vessels are cylindrical tubes with relatively stout walls composed of several layers of various tissues, more especially *elastic tissue* and *smooth muscular fibres*, and the whole is lined by a smooth polished layer of endothelium. One of the most important properties is the **contractility** of the vascular wall, in virtue of which the calibre of the vessel can be varied, and therefore the supply of blood to a part is altered. The contractility is due to the plain muscular fibres, which are, for the most part, arranged circularly. It is most marked in the small arteries, and of course is absent where no muscular tissue occurs. The amount and intensity of the contraction depend upon the development of the muscular tissue; in fact, the two go hand in hand. [If an artery be exposed in the living body it soon contracts under the stimulus of the atmosphere acting upon the muscular fibres. It may also be made to contract by the application of an electrical current, or mechanical stimuli, and in the intact body the vaso-motor nerves govern the muscular fibres.] The contraction takes place slowly, lasts a long time, and has a long latent period like smooth muscle generally.

[Action of Drugs on the Vascular System.]—Gaskell finds that a very dilute solution of lactic acid (1 : 10,000 parts of saline solution), passed through the blood-vessels of a frog, always enlarges the calibre of the blood-vessels, while an **alkaline solution** (1 part sodium hydrate to 10,000 saline solution) always diminishes their size, usually to absolute closure, and indeed the artificial constriction of the blood-vessels may be almost complete. These fluids are antagonistic to each other as far as regards their action on the calibre of the arteries. Dilute alkaline solutions act on the heart in the same way. After a series of beats the ventricle stops beating, the standstill being in a state of contraction. Very dilute lactic acid causes the ventricle to stand still in the phase of complete relaxation. The acid and alkaline saline solutions are antagonistic in their action on the ventricle. Cash and Brunton find that dilute acids have a tendency to increase the transudation through the vessels and produce *œdema* of the surrounding tissues. They also observed that barium, calcium, strontium, copper, iron, and tin produce contraction of the blood-vessels when solutions of their salts are driven through them, while the same effect is produced by very dilute solutions of potassium. Nicotin, atropin, and chloral differ in their action according to the dose. In these experiments the effect was ascertained by the amount of fluid which flowed out of the vessels in a given time.] If blood containing certain drugs be perfused through the blood-vessels of a freshly excised organ, the blood-vessels are **dilated**; e.g., by amyl nitrite, chloral hydrate, morphia, CO, paraldehyde, kairin, quinine, atropin, ferrieyanide of potassium (urea and sodic chloride in the renal vessels),—they are **contracted** by digitalin, veratria, helleborin (*Kobert*). Heat causes contraction of the blood-vessels of the frog's mesentery (*Gärtner*). According to Roy the blood-vessels shorten when heated.

That the **capillaries** undergo expansion and contraction, owing to variations in the size of the protoplasmic elements of their walls, must be admitted.

Stricker has described capillaries as "protoplasm in tubes," and observed that in the tadpole they exhibited movements when stimulated. Golubew described an active state of contraction of the capillary wall, but he regarded the nuclei as the parts which underwent change. Rouget observed the same result in the capillaries of new-born mammals. Tarchanoff found that mechanical or electrical stimulation caused a change in the shape and size of the nuclei, so that

ho regards these as the actively contractile parts. [Sevorini also attaches great importance to the contractility of the capillaries, and especially of their nuclei, as influencing the blood-stream. Oxygen acts on the nuclei of the capillary wall (membrana nictitans of frog) and causes them to swell, while CO_2 has an opposite effect. The circulation through a lung suddenly filled with O or atmospheric air is at first very rapid, but it soon diminishes, while with CO_2 the circulation remains constant.] As the capillaries are excessively thin, soft, and delicate, it is obvious that the form of the individual cells must depend to a considerable extent upon the degree to which the vessels are filled with blood. In vessels which are distended with blood the endothelial cells are flattened, but when the capillaries are collapsed they project more or less into the lumen of the vessel (*Renaut*).

[It is well known that the capillaries present great variations in their diameter at different times. As these variations are usually accompanied by a corresponding contraction or dilatation of the arterioles, it is usually assumed that the variations in the diameter of the capillaries are due to differences of the pressure within the capillaries themselves, viz., to the elasticity of their walls. Every one is agreed that the capillaries are very elastic and extensile, but the experiments of Roy and Graham Brown show that they are contractile as well as elastic, and these observers conclude that, under normal conditions, it is by the contractility of the capillary wall as a whole that the diameter of these vessels is changed, and to all appearance their contractility is constantly in action. "The individual capillaries (in all probability) contract or expand in accordance with the requirements of the tissues through which they pass. The regulation of the vascular blood-flow is thus more complete than is usually imagined." It must be mentioned, however, that some regard the walls of the capillary as playing purely a passive part in the variations of their calibre, although they admit that they are contractile in young animals.]

Physical Properties of Blood-Vessels—Elasticity.—Amongst the physical properties of the blood-vessels, **elasticity** is the most important; their elasticity is *small in amount*, i.e., they offer little resistance to any force applied to them so as to distend or elongate them, but it is *perfect in quality*, i.e., the blood-vessels rapidly regain their original size and form after the force distending them is removed. [An artery, in virtue of its thick elastic walls, when empty or when cut across, does not collapse, but remains open.]

According to E. H. Weber, Volkmann, and Wertheim, the elongation of a blood-vessel (and moist tissues generally) is not proportional to the weight used to extend it, the elongation being relatively less with a large weight than with a small one, so that the curve of extension is nearly [or, at least, bears a certain relation to] a *hyperbola*. According to Wundt, we have not only to consider the extension produced at *first* by the weight, but also the subsequent "elastic after-effect," which occurs gradually. The elongation which takes place during the last few moments occurs so slowly and so gradually that it is well to observe the effect by means of a magnifying lens. Variations from the general law occur to this extent, that if a certain weight is exceeded, less extension, and, it may be, permanent elongation of the artery not infrequently occur. K. Bardeleben found, especially in veins elongated to 40 or 50 per cent. of their original length, that when the weight employed increased by an equal amount each time, the elongation was proportional to the square-root of the weight. This is apart from any elastic after-effect. Veins may be extended to at least 50 per cent. of their length without passing the limit of their elasticity.

[Roy experimented upon the elastic properties of the arterial wall. A portion of an artery, so that it could be distended by any desired internal pressure, was enclosed in a small vessel containing olive oil arranged in the same way as in fig. 72 for the heart. The variations of the contents were recorded by means of a lever writing on a revolving cylinder. The instrument is termed a **sphygmotonometer**. The *aorta and other large arteries* are most elastic and most distensible at pressures corresponding more or less exactly to their normal blood-pressure, while in *veins* the relation between internal pressure and the cubic capacity is very different. In them the maximum of distensibility occurs with pressures immediately above zero. Speaking generally, the cubic capacity of an *artery* is greatly increased by raising the intra-arterial tension, say from zero to about the normal internal pressure which the artery sustains during life. Thus in the *rabbit*, the capacity of the aorta was *quadrupled* by raising the intra-arterial pressure from zero to 200 mm. Hg, while that of the carotid was more than *six times* greater at that pressure than it was in the undistended condition. The pulmonary artery is distinguished by its excessive elastic distensibility. Its capacity (rabbit) was increased more than twelve times on raising the internal pressure from zero to about 36 mm. Hg. Veins, on the other hand, are distinguished by the relatively small increase in their cubic capacity produced by greatly raising the internal pressure, so that the enormous changes in the capacity of the veins during life are due less to differences in the pressure than to the great differences in the *quantity* of blood which they contain.]

Pathological.—Interference with the nutrition of an artery alters its elasticity [and that in

cases where no structural changes can be found]. Marasmus preceding death causes the arteries to become wider than normal. In some old people they become atheromatous and even calcified.

[The **capillaries** by the thinness and permeability of their walls are well adapted for the exchange between the fluids and gases of the blood which they contain, and the tissues lying outside them; while by their extensibility and elasticity they can adapt their calibre to the pressure and quantity of blood within them.]

Uses of Elasticity.—The elasticity of the arteries is of the utmost importance in aiding the conversion of the unequal movement of the blood in the large arteries into a uniform flow in the capillaries. E. H. Weber compared the elastic wall of the arteries with the air in the air-chamber of a fire-engine. In both cases an elastic medium is acted upon—the air in the one case and the elastic tissue in the other—which in turn presses upon the fluid, propelling it onwards continually, while the action of the pump or the heart, as the case may be, is intermittent. The ordinary spray-producer acts on this principle. A uniform spray or jet is obtained by pumping intermittently, but only when the resistance is such as to bring into action the elasticity of the bag between the pump and the spray-orifice.]

Cohesion.—The cohesion of blood-vessels is very great, and in virtue of this they are able to resist even considerable internal pressure without giving way. The carotid of a sheep is ruptured only when fourteen times the usual pressure it is called upon to bear is put upon it (*Volkman*). Given a vein and an artery of the same thickness, a greater pressure is required to rupture the former than the latter. The human carotid or iliac artery resists a pressure of 8 atmospheres, the veins about the half of this.

[**Division of an Artery.**—When an artery is divided in the living body, the blood spouts in jets from the proximal cut end of the tube, *i.e.*, the heart end. Each jet forms a parabolic curve, and the flow does not cease between the jets. If a large artery be severed, the blood may be projected for a distance of several feet, this being greater the larger the artery and the nearer it is to the heart. A very small amount of blood may flow from the distal cut end. This will depend on the extent to which collateral anastomosis takes place.]

[In the case of a **divided vein**, the blood flows chiefly from the distal end, and it does not come in jets, but as a slow continuous flow. The flow from the central end may be almost *nil* or very slight, but this again depends on the amount of collateral circulation.]

[**Ligature of an Artery** ruptures the inner coat, and the vessel swells on the proximal side of the ligature, while immediately after the ligature is applied the distal part of the vessel, *i.e.*, the part beyond the ligature, collapses and becomes smaller, and no pulse is felt in it, while the pulse is felt in the proximal part right up to the ligatured spot.]

[**Ligature of a Vein** causes the vein to swell on the distal side of the ligature, while on the proximal or cardiac side it collapses, unless there be a very free collateral circulation. No pulse is felt on either side of the ligature. These results necessarily follow from the course of the blood-stream—moving as it does in opposite directions—in the two vessels.]

66. INVESTIGATION OF THE PULSE.—[The characters of the pulse may be investigated by—

- (1) The eye (*inspection*).
- (2) The finger (*palpation*).
- (3) Instruments.

The examination is usually confined to that part of the radial artery which lies immediately above the wrist, with the flexor tendons internal to it, and the ridge of the radius on its outer aspect, while the shaft of the radius forms a firm bony support against which the artery can be compressed by means of the finger. When a finger is placed on the radial artery—covered here only by skin and subcutaneous tissue—or on any artery in the living body, one feels a distinct sense of

resistance, which becomes more marked at regular intervals corresponding to each heart-beat. It feels as if the artery expanded somewhat under the finger. This is the *pulse*. One can also feel that in the intervals it seems to recede from the finger. In some situations the pulse can be seen. No such pulse or beat is felt in a vein.]

[Two or three fingers are placed over the course of the radial artery, and the various phenomena in connection with the pulse are noted. It takes much practice for the physician to acquire the *tactus eruditus*, and notwithstanding the value of instruments, every physician should make a careful study of the pulse-beat with his finger. In order to feel the pulse-beat or to take a pulse-tracing, there must be some resistant body, *e.g.*, a bone behind the artery, and a certain degree of pressure must be exerted on the artery.]

The individual phases of the movement of the pulse can only be accurately investigated by the application of **instruments** to the arteries.

(1) **Poiseuille's Box Pulse-Measurer** (1829).—An artery is exposed and placed in an oblong box filled with an indifferent fluid. A vertical tube with a scale attached communicates with the interior of the box. The column of fluid undergoes a variation with every pulse-beat.

(2) **Hérissou's Tubular Sphygmometer** consists of a glass tube whose lower end is covered with an elastic membrane (fig. 83). The tube is partly filled with Hg. The membrane is placed over the position of a pulsating artery, so that its beat causes a movement in the Hg. Chelius used a similar instrument, and he succeeded with this instrument in showing the existence of the double beat (dicrotism) in the normal pulse (1850).

(3) **Vierordt's Sphygmograph** (1855).—In this, one of the earliest sphygmographs, Vierordt departed from the principle of a fluctuating fluid column, and adopted the principle of the *lever*. Upon the artery rested a small pad, which moved a complicated system of levers. At first he used a straw 6 inches long, which rested on the artery. The point of one of the levers inscribed its movements upon a revolving cylinder. This instrument was soon discarded.

(4) **Marey's Sphygmograph** consists of a combination of a lever with an elastic spring. The elastic spring (fig. 84, A) is fixed at one end, *z*, free at the other end, and provided with an ivory pad, *y*, which is pressed by the spring upon the radial artery. On the upper surface of the pad there is a vertically-placed fine-toothed rod, *k*, which is pressed upon by a weak spring, *e*, so that its teeth dovetail with similar teeth in the small wheel, *t*, from whose axis there projects a long, light,

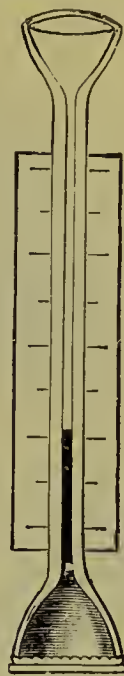


Fig. 83.

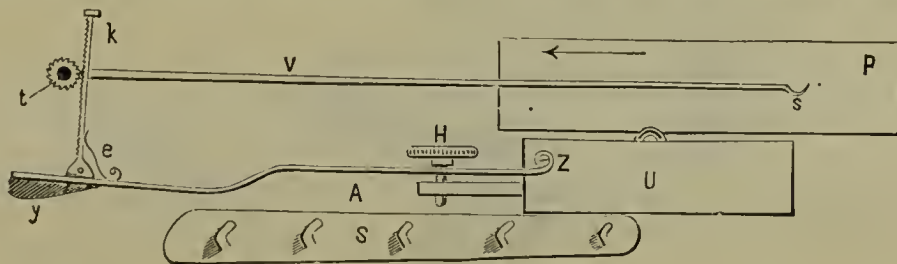


Fig. 84.

Scheme of Marey's sphygmograph. A, spring with ivory pad, *y*, which rests on the artery; *e*, weak spring pressing *k* into *t*; *v*, writing lever; P, piece of smoked glass or paper moved by clock-work, U; H, screw to limit excursion of A; S, arrangement for fixing the instrument to the arm of the patient.

wooden lever, *v*, running nearly parallel with the elastic spring. This lever has a fine style at its free end, *s*, which writes upon a smoked plate, P, moved by clock-work, U, in front of the style. Marey's instrument, as improved by Mahomed and others, has been very largely used.

[Its more complete form, as in fig. 85, where it is shown applied to the arm, consists of—(1) a steel spring, A, which is provided with a pad resting on the artery, and moves with each

movement of the artery ; (2) the lever, C, which records the movement of the artery and spring in a magnified form on the smoked paper, G ; (3) an arrangement, L, whereby the exact pressure exerted upon the artery is indicated on the dial, M ; (4) the clock-work, H, which moves the smoked paper, G, at a uniform rate ; (5) a framework to which the various parts of the instrument are attached, and by means of which the instrument is fastened to the arm by straps, K, K (*Byrom Bramwell*).

[**Application.**—In applying the sphygmograph, cause the patient to seat himself beside a low table, and place his arm on the double-inclined plane (fig. 85). In the newer form of instru-

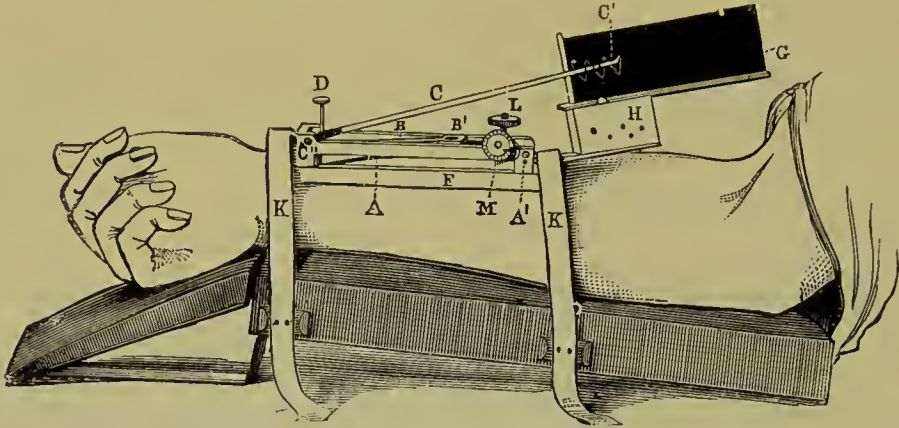


Fig. 85.

Marey's improved sphygmograph. A, steel spring ; B, first lever ; C, writing lever ; C', its free writing end ; D, screw for bringing B in contact with C ; G, slide with smoked paper ; H, clock-work ; L, screw for increasing the pressure ; M, dial indicating the pressure ; K, K, straps for fixing the instrument to the arm, and the arm to the double-inclined plane or support.

ment, the lid of the box is so arranged as to unfold to make this support. The fingers ought to be semi-flexed. Mark the position of the radial artery with ink. See that the clock-work is wound up, and apply the ivory pad exactly over the radial artery where it lies upon the radius,

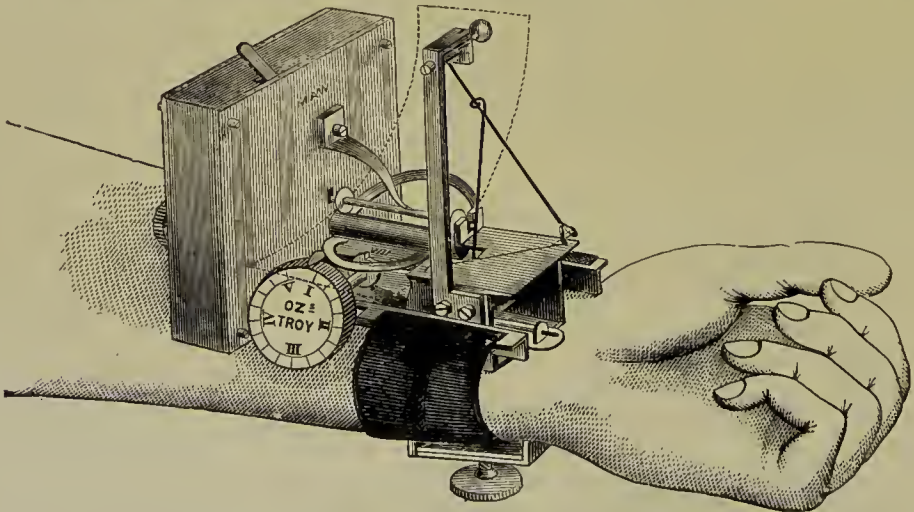


Fig. 86.

Dudgeon's sphygmograph.

fixing it to the arm by the non-elastic straps, K, K. Fix the slide holding the smoked paper in position. The best paper to use is that with a very smooth surface, or an enamelled card smoked over the flame of a turpentine lamp, over a piece of burning camphor, or over a fan-tailed gas-burner. The writing-stylo is so arranged as to write upon the smoked paper with the least possible friction. It is most important to regulate the pressure exerted upon the

artery by means of the milled head, *L*. This must be determined for each pulse, but the rule is to graduate the pressure until the greatest amplitude of movement of the lever is obtained. Set the clock-work going, and a tracing is obtained, which must be "fixed" by dipping it in

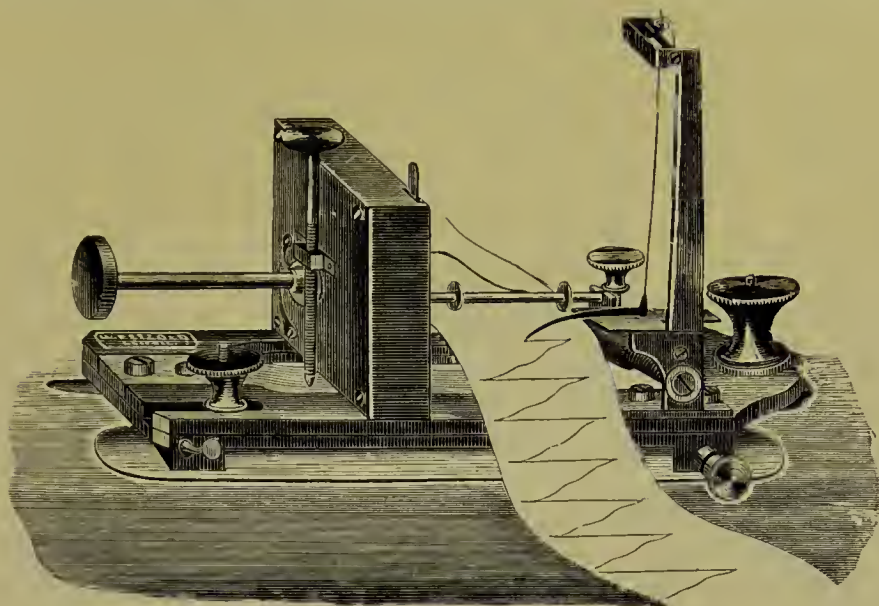


Fig. 87.

Ludwig's sphygmograph.

a rapidly drying varnish, *e.g.*, photographic. In every case scratch on the tracing with a needle the name, date, and amount of pressure employed.]

[(5) Dudgeon's Sphygmograph.—This is a convenient form of sphygmograph, although

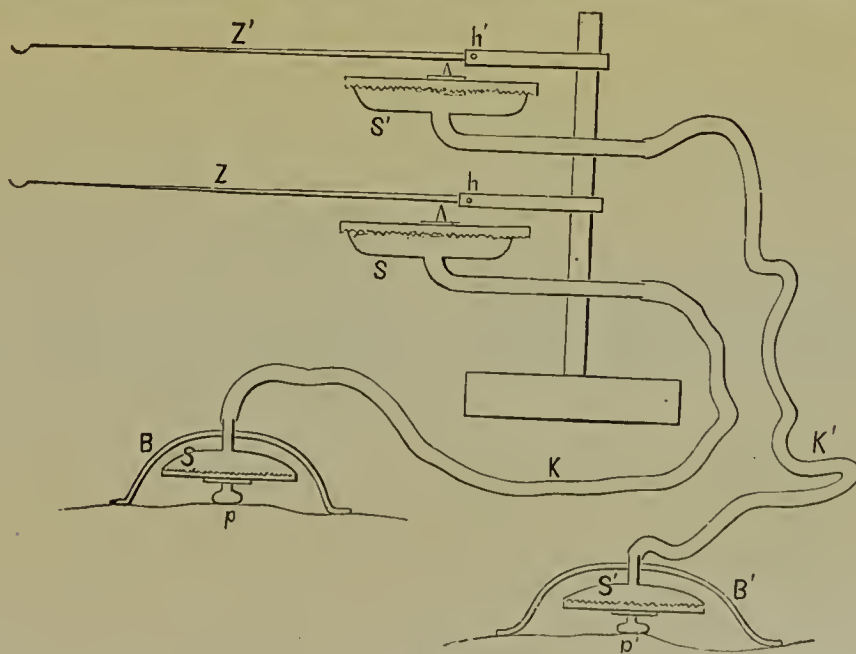


Fig. 88.

Scheme of Brondgeest's sphygmograph. *S S'*, receiving and recording (*S, S'*) tambours with writing levers, *Z* and *Z'*; *K, K'*, conducting tubes: *p*, over heart, *p'*, over a distant artery.

Broadbent and Roy regard its results as untrustworthy. The instrument after being carefully adjusted upon the radial artery is kept in position by an inelastic strap. The pressure of the

spring is regulated by the eccentric wheel to any amount from 1 to 5 ounces. As in other instruments, the tracing paper is moved in front of the writing-needle by means of clock-work. The writing levers are so adjusted that the movements of the artery are magnified fifty times (fig. 86).]

[(6) Ludwig's improved form is a very serviceable instrument (fig. 87).]

(7) Marey's tambours are also employed for registering the movements of the pulse. They are used in the same way as the pansphygmograph. Two pairs of metallic cups (fig. 88, S, S, and S', S', Upham's capsules) are pierced in the middle by thin metal tubes, whose free ends are connected with caoutchouc tubes, K and K'. All the four metallic vessels are covered with elastic membranes. On S and S' are fixed two knob-like pads, *p* and *p'*, which are applied to the pulsating arteries, and the metal arcs, B and B', retain them in position. On the other tambours are arranged the writing-levers, Z and Z'. Pressure on the one tambour necessarily compresses the air, and makes the other, with which it is connected, expand, so as to move the writing-lever. This arrangement does not give absolutely exact results; still, it is very easily used, and is convenient. In fig. 88 a double arrangement is shown, whereby one instrument, B, may be placed over the heart, and the other, B', on a distant artery.

(8) Landois' Angiograph.—To a basal plate (fig. 89), G G, are fixed two upright supports, *p*, which carry between them at their upper part the movable lever, *d*, *r*, carrying a rod bearing a pad, *e*, directed downwards, which rests on the pulse. The short arm carries a counterpoise, *d*,

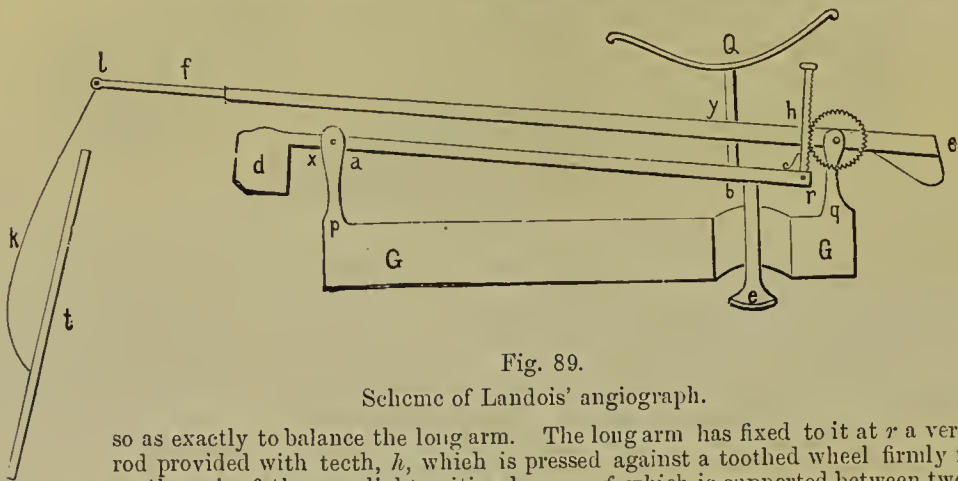


Fig. 89.

Scheme of Landois' angiograph.

so as exactly to balance the long arm. The long arm has fixed to it at *r* a vertical rod provided with teeth, *h*, which is pressed against a toothed wheel firmly fixed on the axis of the very light writing-lever, *e*, *f*, which is supported between two uprights, *q*, fixed to the opposite end of the basal plate, G, G. The writing-lever is equilibrated by means of a light weight. The writing-needle, *k*, is fixed by a joint to *e*, and it writes on the plate, *t*. The first-mentioned lever, *d*, *r*, carries a shallow cup, Q, just above the pad, into which weights may be put to press on the pulse. In this instrument the weight can be measured and varied; the writing-lever moves vertically, and not in a curve as in Marey's apparatus, which greatly facilitates the measuring of the curves (fig. 89).

Other sphygmographs are used, both in this country and abroad, including that of Sommerbrodt, which is a complicated form of Marey's sphygmograph, and those of Pond and Mach.

[Whatever the form of the sphygmograph, the pressure is applied to the artery either by means of a spring (Marey, Dudgeon, &c.) or by actual weights which press upon the artery (Sommerbrodt, Landois). In Marey's form the lever moves in an arc of a circle on the paper so that the upstroke has always a backward inclination, while in Sommerbrodt's the lever moves at right angles to the paper, and makes a vertical line. Thus the form of the curve obtained will vary to a certain extent with the sphygmograph employed. As a matter of fact, the sphygmograph does not aid one so much in diagnosis as has been claimed for it. It, however, accentuates certain phenomena, which cannot be so well studied with the unaided fingers.]

In every pulse-curve—sphygmogram or arteriogram—we can distinguish the *ascending part* (ascent) of the curve, the *aper*, and the *descending part* (descent). Secondary elevations scarcely ever occur in the ascent, which is usually represented by a straight line, while they are always present in the descent (fig. 91). Such elevations occurring in the descent are called **catacrotic**, and those in the ascent, **anacrotic**. When the recoil elevation or dicrotic wave occurs in a well-marked form in the descent, the pulse is said to be **dicrotic**, and when it occurs twice, **tricrotic**.

Measuring Pulse-Curves.—If the smoked surface on which the tracing is inscribed is moved

at a uniform rate by means of the clock-work, then the height and length of the curve are measured by means of an ordinary rule. If we know the rate at which the paper was moved, then it is easy to calculate the duration of any event in the curve.

Gas-Sphygmoscope.—A small metallic or glass capsule provided with an inlet and an outlet tube, and closed below by a fine membrane, is placed over an artery. The inlet tube is connected to a gas supply, and the outlet to a rat-tailed gas-burner. The gas-jet responds to every pulse-beat. Czermak photographed a beam of light set in motion by the movements of the pulse.

Hæmautography.—Expose a large artery of an animal, and divide it so that the stream of blood issuing from it strikes against a piece of paper drawn in front of the blood-stream. The curve so obtained (fig. 90) shows, in addition to the primary wave, P, a distinct dicrotic wave R, and slight vibrations, *e, e*, due to the variations in the elasticity of the arterial wall, which shows that the movements occur in the blood itself, and are communicated as waves to the arterial wall. By estimating the amount of blood in the various parts of the curve, we obtain a knowledge of the amount of blood discharged by the divided artery during the systole and diastole (*i.e.*, the narrowing and dilatation) of the artery—the ratio is 7 : 10. Thus in the *unit of time*, during arterial dilatation, rather more than *twice* as much blood flows out as compared with what occurs during arterial contraction.

67. PULSE-TRACING OR SPHYGMOGRAM.

—[**The Pulse.**—With each systole of the heart, a certain quantity of blood is forced into the already filled and partially distended arteries, the resistance in the vessels is lowest between the pulsations, and at this time the arterial tubes are somewhat flattened, but with each systole of the left ventricle the pulse-wave, or rather the liquid pressure within the vessel, is increased, thus forcing the artery back into the circular form. “The change of shape, from the flattened condition impressed upon the vessel by the finger or the sphygmograph lever, to the round cylindrical shape which it assumes under the distending force of the blood within it, constitutes the pulse,” and it indicates the degree and dura-

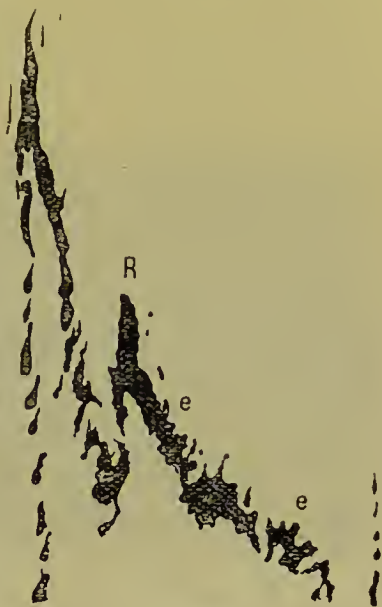
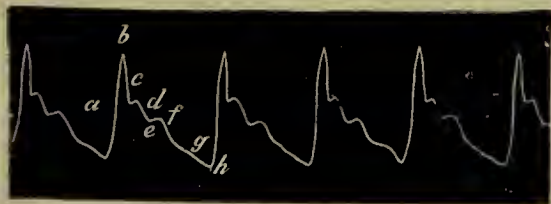


Fig. 90.

Hæmautographic curve of the posterior tibial artery of a dog. P, primary pulse-wave; R, dicrotic wave; *e, e*, elevations due to elasticity.



A



B

Fig. 91.

A, Pulse-tracing by Dudgeon's sphygmograph. Sphygmogram of radial artery : pressure 2 oz. Each part of the curve between the base of one up-stroke and the base of the next up-stroke corresponds to a beat of the heart, so that this figure shows five heart-beats and part of a sixth. B, Normal pulse-tracing taken with Marey's sphygmograph : pressure $2\frac{1}{2}$ oz.

tion of the increased pressure in the arterial system caused by the ventricular systole (*Broadbent*.)]

Analysis.—A sphygmogram or pulse-tracing consists of a series of curves (figs. 91, 92) each of which corresponds with one beat of the heart. Each pulse-curve consists of—

1. The line of ascent (*a* to *b* in fig. 91).
2. The apex (*P* in fig. 94, and *b* in fig. 91).
3. The line of descent (*b* to *h* in fig. 91).

(1) The **line of ascent**, or **up-stroke**, is nearly vertical, and occurs during the dilatation of the artery produced by the systole of the left ventricle, when the aortic valves are forced open and the ventricular contents are projected into the arterial system. [The ascent is a nearly vertical, uninterrupted line, but in some cases, where the ventricle contracts very suddenly, as occasionally happens in aortic regurgitation, it is quite vertical (fig. 97).]

(2) The **apex** or **percussion wave** in a normal pulse is pointed.

(3) The **line of descent** is gradual, and corresponds to the diminution of diameter or more gradual contraction of the artery after the cessation of the cardiac systole. It is interrupted

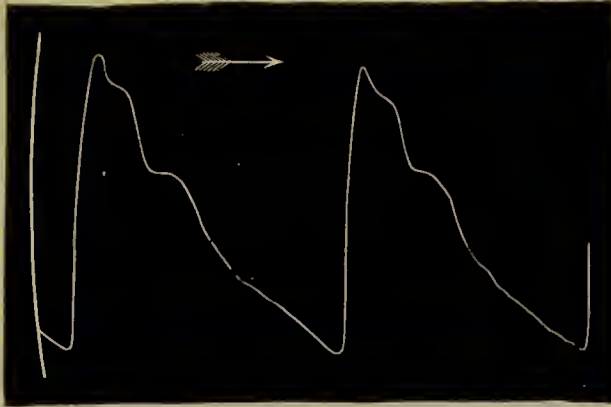


Fig. 92.

Radial pulse-tracing by Roy and Adami's method.

Extra-vascular pressure = 100 mm. Hg.

by two completely distinct elevations of secondary waves. Such elevations are called "catacrotic." The more distinct of the two occurs as a well-marked elevation about the middle of the descent (R in fig. 94 and *f* in fig. 91); it is called the **dicrotic wave**, or, with reference to its mode of origin, the "*recoil wave*." [As the descent corresponds to the time when blood is flowing out of the arteries at the periphery into the capillaries, its direction will depend on the rapidity of the outflow. Thus it will be more rapid in paralysis of the arterioles

and very rapid in aortic regurgitation, where, of course, much of the blood flows backward into the left ventricle (fig. 97). In this case, the artery will recoil suddenly from under the finger or pad of the instrument, and this constitutes the "pulse of empty arteries."]

The **dicrotic wave**, or **recoil wave**, corresponds to the time following the closure of the aortic valves, and is preceded in the descent by a slight depression, the **aortic notch**.

[The **tidal**, or **pre-dicrotic wave**, occurs between the apex and the dicrotic wave (fig. 91, *d*). It occurs on the descent, and during the contraction of the ventricle. The tidal wave is best marked in a *hard* pulse, *i.e.*, where the blood-pressure is high, so that it is usually well marked in cirrhotic disease of the kidney, accompanied by hypertrophy of the left ventricle.]

There may be other **secondary** waves in the lower part of the descent.

[**Respiratory** or **Base Line**.—If a line be drawn so as to touch the bases of all the up-strokes, we obtain a straight line, hence called by this name. The base line is altered in disease and during forced respiration (§ 74).]

[Pulse-tracings obtained in different ways from different animals and man resemble each other in that they all show an uninterrupted rapid up-stroke, culminating in the point of the curve which forms the percussion-wave or first secondary wave of the pulse. Between the apex and the next small wave is a notch, the pre-dicrotic notch, followed immediately by the tidal wave. After this is the deeper dicrotic notch, and then the dicrotic wave. This is followed by a more or less prominent short wave, between which and the lowest part of the curve is a large flattened wave.]

[Roy and Adami adopt a somewhat different terminology, based on the views they hold as to the cause of the several parts of a pulse-tracing. The term **up-stroke** is retained, but the percussion-wave they call the **papillary wave** or first secondary

wave. According to them, it is due to the contraction of the papillary muscles, and results from the rise of pressure due to contraction of the papillary muscles. The next secondary or tidal wave they call **outflow remainder wave**, and it corresponds in time with the outflow from the ventricles, and with it the outflow from the ventricles terminates. After this comes the **dicrotic notch**, which they ascribe to "the inertia of the blood in the aorta and larger arteries, which has gained a certain velocity during the period of outflow from the ventricle, and which upon the blood ceasing to leave the ventricle necessarily causes a negative wave, commencing at the root of the aorta, and propagated in the same direction as the positive wave." Then follows the **dicrotic wave**, which they ascribe to inertia, and then the long slow descent marked by a rounded shoulder, and perhaps another small inertia wave.]

[In some cases, *e.g.*, **mitral regurgitation**, the pre-dicrotic wave may be present in some pulse-beats and absent in others (fig. 93), where the tidal wave is present in the largest pulse, and absent in the others, while the base line is uneven. In mitral stenosis the amount of blood discharged into the left ventricle frequently varies, hence the variations in the characters of the arterial pulse.]

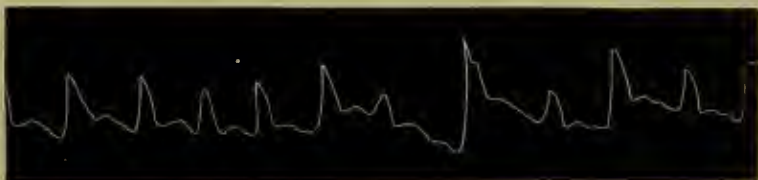


Fig. 93.

Irregular pulse of mitral regurgitation.

The pulse-curve indicates the variations of pressure which the blood exerts on the arterial walls, for the lever rises and falls with the pressure, hence v. Kries calls it the "pressure-pulse."

68. ORIGIN OF THE DICROTIC WAVE.—The **dicrotic**, or **recoil wave**, which is always present in a normal pulse, is caused thus:—During the ventricular systole a mass of blood is propelled into the already full aorta, whereby a positive wave is rapidly transmitted from the aorta throughout the arterial system, even to the smallest arterioles, *in which this primary wave is extinguished*. As soon as the semi-lunar valves are closed, and no more blood flows into the arterial system, the arteries, which were previously distended by the mass of blood suddenly thrown into them, recoil or contract, so that in virtue of the elasticity (and contractility) of their walls, they exert a counter-pressure upon the column of blood, and thus the blood is forced onwards. There is a free passage for it towards the periphery, but towards the centre (heart) it impinges upon the already closed semi-lunar valves. This develops a new positive wave, which is propagated peripherally through the arteries, where it disappears in their finest branches. In those cases where there is sufficient time for the complete development of the pulse-curve (as in the short course of the carotids, and in the arteries of the upper arm, but not in those of the lower extremity, on account of their length), a second reflected wave may be caused in exactly the same way as the first. Just as the pulse occurs later in the more peripherally placed arteries than in those near the heart, so the secondary wave reflected from the closed aortic valves must appear later in the peripheral arteries. Both kinds of waves, the primary pulse-wave, the secondary, and eventually even the tertiary reflected wave—arise in the same place, and take the same course, and the longer the course they have to travel to any part of the arterial system, the later they arrive at their destination.

[Amongst the conditions which favour dicrotism are low blood-pressure and a rapid sharp cardiac contraction. When the blood-pressure is low, there is less resistance to the inflow of blood at the aorta from the left ventricle, so that its systole occurs sharply, forcing on the blood and distending the arterial walls. The elastic coats rebound on the contained blood, and thus start a wave from the closed semi-lunar valves.]

[Roy and Adami have shown that increased depth of the dicrotic notch is obtained "by any cause which diminishes the volume of blood which is thrown out by the ventricle at each con-

traction, and (contrary to the usual teaching on this subject), also by any cause which, *ceteris paribus*, raises the pressure within the systemic arteries. Again, a pulse-wave with greatly increased dierotism may occur with intra-arterial pressures at or above the normal." There are, however, differences between the increased dierotism of high and of low pressure. From this it

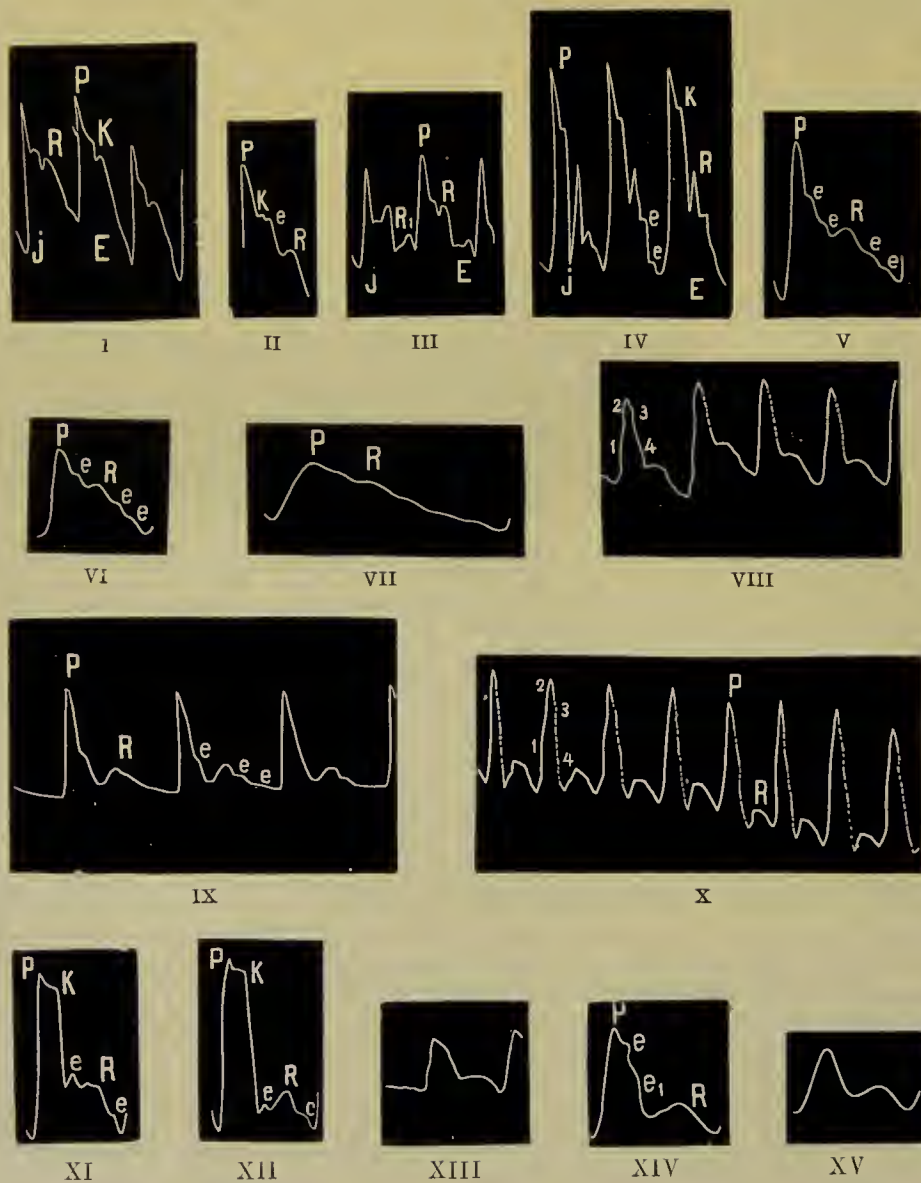


Fig. 94.

I, II, III, sphygmograms of carotid artery; IV, axillary; V to IX, radial; X, dierotic radial pulse; XI, XII, eural; XIII, posterior tibial; XIV, XV, pedal. In all the curves P indicates apex; R, dierotic wave; e, e, elevations due to elasticity; K, elevation caused by the closure of the semi-lunar valves of the aorta.

follows that the mere form of the pulse-wave is not a safe guide to the height of the medium arterial pressure.]

The following points regarding the dierotic wave have been ascertained experimentally, chiefly by Landois:—

1. The dierotic wave occurs later in the descending part of the curve, the further the artery experimented upon is distant from the heart. Compare the curves, fig. 94.

The shortest accessible course is that of the carotid; where the dirotic wave reaches its maximum 0·35 to 0·37 sec. after the beginning of the pulse. In the upper extremity the apex of the dirotic wave is 0·36 to 0·38 or 0·40 sec. after the beginning of the pulse-beat. The longest course is that of the arteries of the lower extremity. The apex of the dirotic wave occurs 0·45 to 0·52 or 0·59 sec. after the beginning of the curve. It varies with the height of the individual.

2. The dirotic elevation in the descent is lower, and is less distinct, the further the artery is situated from the heart, so that the longer the distance which the wave has to travel the less distinct it becomes.

3. It is best marked in a pulse where the primary pulse-wave is short and energetic. It is greatest relatively when the systole of the heart is short and energetic.

4. It is better marked *the lower the tension* of the blood within the arteries, [and is best developed in a *soft* pulse]. In fig. 94, IX and X were obtained when the tension of the arterial was *low*; V and VI, *medium*; and VII with *high* tension.

[**Soft and Hard Pulse.**—A soft pulse may be one with low arterial tension; in a hard pulse the tension is high. In a soft pulse the dirotic wave is always well marked, and the tidal wave small or absent. In a soft pulse and pulse of low

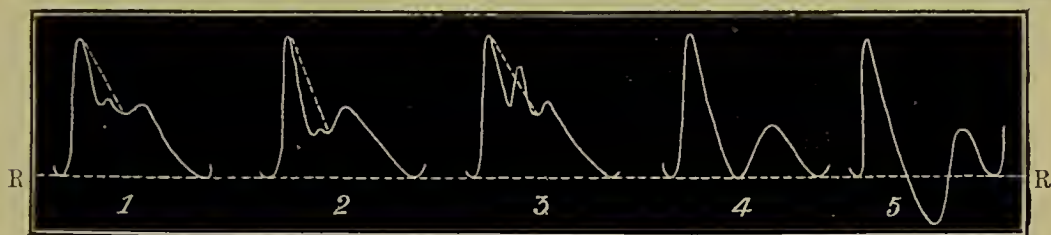


Fig. 95.

Schemata of pulse-tracings. 1, normal; 2, low tension and soft pulse; 3, high tension and hard pulse; 4, soft pulse fully dirotic; 5, very soft pulse and hyperdirotic; R, respiratory or base line. The dotted line is put in to show the relation of the tidal wave.

tension, if a line be drawn from the apex of the sphygmogram to the lowest point of the aortic notch, the tidal wave, if present at all, falls below this line, as in the diagram (fig. 95).

In a hard pulse the tension is high, and the tidal wave is well marked, extending above a line drawn from the apex to the lowest point of the aortic notch.]

Conditions influencing Arterial Tension.—It is diminished at the beginning of inspiration (§ 74), by hæmorrhage, stoppage of the heart, heat, an elevated position of parts of the body, amyl nitrite, nitro-glycerin, and the nitrites generally. [Both drugs accelerate the pulse-beats and produce marked dirotism; with amyl nitrite the full effect is obtained in from 15 to 20 sec. after the inhalation of the dose (fig. 96, A, A'), but with nitro-glycerin not until 6 or 7

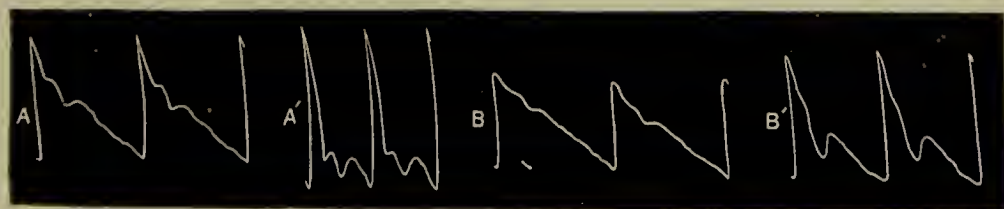


Fig. 96.

Pulse-tracings. A, normal; A', one minute after inhalation of amyl nitrite; B, normal; B' after a dose of nitro-glycerine (*Stirling after Murrell*).

min. (fig. 96, B, B') and in the latter case the effects last longer.] It is increased at the beginning of expiration by accelerated action of the heart, stimulation of vaso-motor nerves, diminished outflow of blood at the periphery, and by inflammatory congestion due to certain poisons, as lead; compression of other large arterial trunks, action of cold and electricity on the small cutaneous vessels, and by impeded outflow of venous blood. When a large arterial trunk is exposed, the stimulation of the air causes it to contract, resulting in an increased

tension within the vessel. In many diseased conditions the arterial tension is greatly increased—[e.g., in Bright's disease, where the kidney is contracted ("granular"), and where the left ventricle is hypertrophied.]

In all these conditions increased arterial tension is indicated by the dicrotic wave being less high and less distinct, while with diminished arterial tension it is a larger and apparently more independent elevation. Moens has shown that the time between the primary elevation and the dicrotic wave increases with increase in the diameter of the tube, with diminution of its thickness, and when its coefficient of elasticity diminishes.

[The dicrotic wave is absent or but slightly marked in cases of atheroma and in aortic regurgitation (fig. 97). In this fig. observe also the vertical character of the up-stroke.]

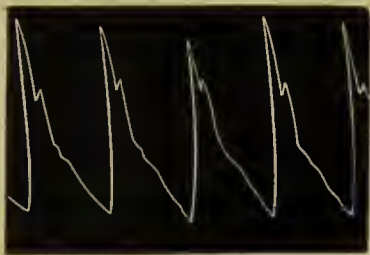


Fig. 97.

Aortic regurgitation.

Elastic Elevations.—Besides the dicrotic wave, a number of small less-marked elevations occur in the course of the descent in a sphygmogram (fig. 94, e, e). These elevations are caused by the elastic tube being thrown into vibrations by the rapid energetic pulse-wave, just as an elastic membrane vibrates when it is suddenly stretched. The artery also executes vibratory movements when it passes suddenly from the distended to the relaxed condition. These small elevations in the pulse-curve, caused by the elastic vibrations of the arterial

wall, are called "**elastic elevations**" by Landois.

(1) The elastic vibrations increase in number in one and the same artery with the degree of tension of the elastic arterial wall. A very high tension occurs in the cold stage of intermittent fever, in which case these elevations are well marked.

(2) If the tension of the arterial wall be greatly diminished, these elevations may disappear, so that, while diminished tension favours the production of the dicrotic wave, it acts in the opposite way with reference to the "elastic elevations." (3) In diseases of the arterial walls affecting their elasticity, these elevations are either greatly diminished or entirely abolished. (4) The farther the arteries are distant from the heart, the higher are the elastic elevations. (5) When the mean pressure within the arteries is increased by preventing the outflow of blood from them, the elastic vibrations are higher and nearer the apex of the curve. (6) They vary in number and length in the pulse-curves obtained from different arteries of the body.

When the arm is held in an upright position, after five minutes the blood-vessels empty themselves, and collapse, while the elasticity of the arteries is diminished.

69. Dicrotic Pulse.—Sometimes during fever, especially when the temperature is high, a dicrotic pulse may be felt, each pulse-beat, as it were, being composed of two beats (fig. 94, X), one beat being large and the other small, and more like an after-beat. Both beats correspond to *one* beat of the heart. The two beats are quite distinguishable by the touch. The phenomenon is only an exaggerated condition of what occurs in a normal pulse. *The sensible second beat is nothing more than the greatly increased dicrotic elevation*, which, under ordinary conditions, is not felt by the finger.

Conditions for dicrotism.—The occurrence of a dicrotic pulse is favoured (1) by a short primary pulse-wave, as in fevers, where the heart beats rapidly.

(2) By *diminished arterial tension*. A short systole and diminished arterial blood-pressure are the most favourable conditions for causing a dicrotic pulse. [So that dicrotism is best marked in a soft pulse (p. 120).] The double beat may be felt only at certain parts of the arterial system, whilst at other parts only a single beat is felt. A favourite site is the radial artery of one or other side, where conditions favourable to its occurrence appear to exist. This seems to be due to a local diminution of the blood-pressure in this area, owing to the paralysis of its vaso-motor nerves (Landois). If the tension be increased by compressing other large arterial trunks or the veins of the part, the double beat becomes a simple pulse-beat. The dicrotic pulse in fever seems to be due to the increased temperature (39° to 40° C.), whereby the artery is more distended, and the heart-beat is shorter and more prompt.

(3) It is absolutely necessary that the *elasticity of the arterial wall be normal*. The dicrotic pulse does not occur in old persons with atheromatous arteries.

Monocrotic Pulse.—In fig. 98, A, B, C, we observe a gradual passage of the normal radial curve, A, into the dicrotic beat, B, and C, where the dicrotic wave, *r*, appears as an independent

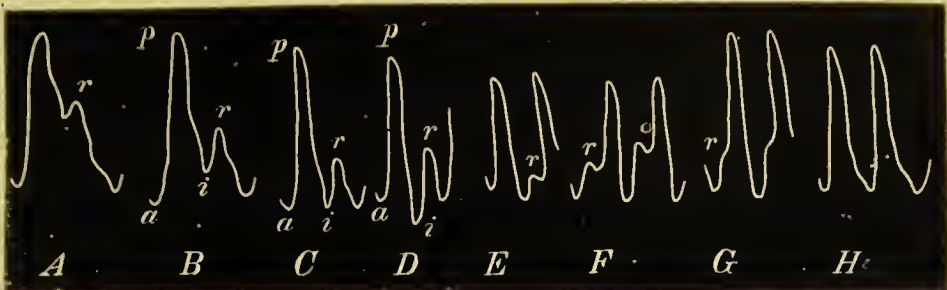


Fig. 98.
Development of the Pulsus dicrotus—P. caprizans ; P. monocrotus.

elevation. If the frequency of the pulse increases more and more in fever, the next following pulse-beat may occur in the ascending part of the dicrotic wave, D, E, F, and it may be even close to the apex of the latter (G) (P. caprizans). If the next following beat occurs in the depression, *i*, between the primary elevation, *p*, and the dicrotic elevation, *r*, the latter entirely disappears, and the curve, H, assumes what Laudois calls the “monocrotic” type.

[**Degrees of Dicrotism.**—When the aortic notch reaches the respiratory or base line, the tidal wave having disappeared, the pulse is said to be fully dicrotic (fig. 95.). When the aortic notch falls below the base line, *i.e.*, below where the up-stroke begins, the pulse is said to be hyperdicrotic (figs. 95, 99). This form occurs during high fever (104° F.), and is usually a grave sign, indicating exhaustion and the need for stimulants.]

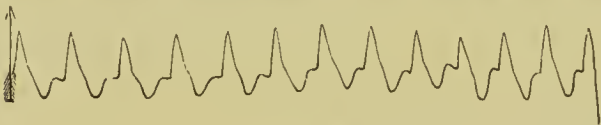


Fig. 99.
Hyperdicrotic pulse.

70. CHARACTERS OF THE PULSE.—[The three factors concerned in the production of the pulse are, (1) the action of the heart, (2) the elasticity of the large vessels, (3) the resistance in the small arteries and capillaries. Any or all or several of these factors may be modified.]

- (1) **Frequency.**—According as a greater or less number of beats occurs in a given time, *e.g.*, per minute, the pulse is said to be frequent or infrequent. The normal rate, in man=71 per minute, and somewhat more in the female; in fever it may exceed 120 (250 have been counted by Bowles), while in other diseases it may fall to 40, and even 10 to 15; but such cases are rare and are probably due to an affection of the cardiac nerves (§ 41). The frequency of the pulse is usually increased when the respirations are deeper, but not more numerous, *i.e.*, rapid shallow respirations do not affect the frequency of the pulse, but deep respirations do. [The frequency may be regular or irregular with regard to time.]
- (2) **Celerity or Rapidity.**—If the pulse-wave is developed, so that the distention of the artery slowly reaches its height, and the relaxation also takes place gradually, we have the *p. tardus* or *slow* or *long* pulse; the opposite condition gives rise to the *p. celer* or *quick* or *short* pulse. The rapidity of the pulse is increased by quick action of the heart, power of expansion of the arterial walls, easy efflux of blood owing to the dilatation of the small arteries, and by nearness to the heart. [The *quickness* has reference to a *single* pulse-beat, the *frequency* to a *number* of beats.] In a quick pulse, the curve is high and the angle at the apex is acute, while in a slow pulse the ascent is low and the angle at the apex is large.
- (3) **Conditions affecting the Pulse-Rate.**—**Frequency in Health.**—In man the normal pulse-rate=71 to 72 beats per minute, in the female about 80. In some individuals the pulse-rate may be higher (90 to 100), in others lower (50), and such a fact must be borne in mind.

(a) Age :—

	Beats per Minute.		Beats per Minute.		Beats per Minute.
Newly born,	130 to 140	5 years,	94 to 90	25 to 50 years,	70
1 year,	120 to 130	10 „	about 90	60 years,	74
2 years,	105	10 to 15 years,	78	80 „	79
3 „	100	15 to 20 „	70	80 to 90 years,	over 80
4 „	97	20 to 25 „	70		

(b) The length of the body has a certain relation to the frequency of the pulse. The following results have been obtained by Czarnecki from the formulæ of Volkmann and Rameaux:—

Length of Body in cm.	Pulse.		Length of Body in cm.	Pulse.	
	Calculated.	Observed.		Calculated.	Observed.
80 to 90, ...	90	103	140 to 150, ...	69	74
90 to 100, ...	86	91	150 to 160, ...	67	68
100 to 110, ...	81	87	160 to 170, ...	65	65
110 to 120, ...	78	84	170 to 180, ...	63	64
120 to 130, ...	75	78	Above 180, ...	60	60
130 to 140, ...	72	76			

(c) The pulse-rate is increased by muscular activity, by every increase of the arterial blood-pressure, by taking of food, increased temperature, painful sensations, by psychical disturbances, and [in extreme debility]. Increased heat, fever, or pyrexia increases the frequency, and as a rule the increase varies with the height of the temperature. [Dr Aitken states that an increase of the temperature of 1° F. above 98° F. corresponds with an increase of ten pulse-beats per minute; thus—

Temp. F.	Pulse-Rate.	Temp. F.	Pulse-Rate.	Temp. F.	Pulse-Rate.
98°	60	101°	90	104°	120
99°	70	102°	100	105°	130
100°	80	103°	110	106°	140

This is merely an approximate estimate.] It is more frequent when a person is *standing* than when he lies down. *Music* accelerates the pulse and increases the blood-pressure in dogs and men. Increased barometric pressure diminishes the frequency.

The Variation of the Pulse-Rate during the Day.—3 to 6 A.M. = 61 beats; 8 to 11½ A.M. = 74. It then falls towards 2 P.M.; towards 3 (at dinner-time) another increase takes place and goes on until 6 to 8 P.M. = 70; and it falls until midnight = 54. It then rises again towards 2 A.M., when it soon falls again, and afterwards rises as before towards 3 to 6 A.M.

[Pulse-Rate in Animals.—(Colin).]

	Per Min.		Per Min.		Per Min.
Elephant, ...	25–28	Lioness, ...	68	Rabbit, ...	120–150
Camel, ...	28–32	Tiger, ...	74	Mouse, ...	120
Giraffe, ...	66	Sheep, ...	70–80	Goose, ...	110
Horse, ...	36–40	Goat, ...	70–80	Pigeon, ...	136
Ox, ...	45–50	Leopard, ...	60	Hen, ...	140
Tapir, ...	44	Wolf (female), ...	96	Snake, ...	24
Ass, ...	46–50	Hyæna, ...	55	Carp, ...	20
Pig, ...	70–80	Dog, ...	90–100	Frog, ...	80
Lion, ...	40	Cat, ...	120–140	Salamander, ...	77]

(4) **Variations in the Pulse-Rhythm (Allorhythmia).**—On applying the fingers to the normal pulse, we feel beat after beat occurring at apparently equal intervals. Sometimes in a normal series a beat is omitted = *pulsus intermittens*, or *intermittent pulse*. [In feeling an inter-

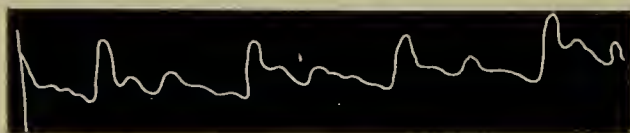


Fig. 100.

Pulsus alternans.

mittent pulse, we imagine or have the impression that a beat is omitted. This may be due to a reflex arrest of the ventricular contraction, caused by digestive derangement, in which case it has no great significance; but if it be due to failure of the ventricular action, intermittent pulse is a serious symptom, being frequently present

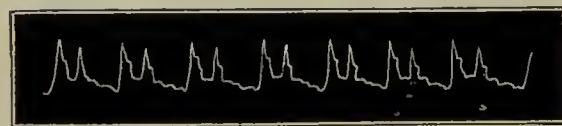


Fig. 101.

Pulsus bigeminus.

when the muscular walls are degenerated.] At other times the beats become smaller and smaller, and after a certain time begin as large as before = *p. myurus*. When an extra beat is intercalated in a normal series = *p. intercurrents*. The regular alternation of a high and a low beat = *p. alternans* (fig. 100). In the *p. bigeminus* of Traube the beats occur in pairs, so that there is a longer pause after every two beats (fig. 101). Traube found that he could produce this form of pulse in eunurised dogs by stopping the artificial respiration for a long time. The *p. trigeminus* and *quadrigeminus* occur in the same way, but the irregularities occur after every third and fourth beat. Knoll found that in animals such irregularities of the pulse were apt to occur, as well as great irregularity in the rhythm generally when there is much resistance to the circulation, and consequently the heart has great demands upon its energy. The same occurs in man where an improper relation exists between the force

of the cardiac muscle and the work it has to do (*Riegel*). Complete irregularity of the heart's action is called *arrhythmia cordis*.

71. VARIATIONS IN THE CHARACTERS OF THE PULSE.—Compressibility.—The relative strength or compressibility of the pulse (*p. fortis* and *debilis*), *i.e.*, whether the pulse is *strong* or *weak*, is estimated by the weight which the pulse is able to raise. A sphygmograph, provided with an index indicating the amount of pressure exerted upon the spring pressing upon the artery, may be used (fig. 85). In this case, as soon as the pressure exerted upon the artery overcomes the pulse-beat, the lever ceases to move. *The weight employed indicates the strength of the pulse.* [The finger may be, and generally is used. The finger is pressed upon the artery until the pulse-beat in the artery *beyond* the point of pressure is obliterated. In health it requires a pressure of several ounces to do this. Handfield Jones uses a *sphygmometer* for this purpose. It is constructed like a cylindrical letter-weight, and the pressure is exerted by means of a spiral spring which has been carefully graduated.] The pulse is *hard* or *soft* when the artery, according to the mean blood-pressure, gives a feeling of greater or less resistance to the finger, and this quite independent of the energy of the individual pulse-beats (*p. durus* and *mollis*). In estimating the *tension* of the artery and the pulse, *i.e.*, whether it is *hard* or *soft*, it is important to observe whether the artery has this quality only during the pulse-wave, *i.e.*, if it is hard during diastole, or whether it is hard or soft during the period of rest of the arterial wall. All arteries are harder and less compressible during the pulse-beat than during the period of rest, but an artery which is very hard during the pulse-beat may be hard also during the pause between the pulse-beats; or it may be very soft, as in insufficiency of the aortic valves. In the latter case, after the systole of the left ventricle, owing to the incompetency of the aortic semi-lunar valves, a large amount of blood flows back into the ventricle, so that the arteries are thereby suddenly rendered partially empty. [The sudden collapse of the artery gives rise to the characteristic “pulse of unfilled arteries” (fig. 97), sometimes also called “Corrigan’s pulse.”]

Under similar conditions, the *volume* of the pulse is obvious from the size of the sphygmogram, so that we speak of a *large* and a *small* or *thready* pulse (*p. magnus* and *parvus*). Sometimes the pulse is so thready and of such diminished volume that it can scarcely be felt. A *large* pulse occurs in disease when, owing to hypertrophy of the left ventricle, a large amount of blood is forced into the aorta. A *small* pulse occurs under the opposite condition, when a small amount of blood is forced into the aorta, either from a diminution of the total amount of the blood, or from the aortic orifice being narrowed [aortic stenosis], or from disease of the mitral valve; again, where the ventricle contracts feebly, the pulse becomes small and thready.

Compare the *two radials*. Sometimes the pulse differs on the two sides, or it may be absent on one side. [The pulse-wave in the two radials is often different when an aneurism is present on one side.]

Angiometer.—Waldenburg constructed a “pulse-clock” to register the tension, the diameter of the artery, and the volume of the pulse upon a dial. It does not give a graphic tracing, the results being marked by the position of an indicator.

72. THE PULSE-CURVES OF VARIOUS ARTERIES.—1. *Carotid* (fig. 94 I, II, III; fig. 94, C and C₁). The ascending part is very steep—the apex of the curve (fig. 94, P) is sharp and high. Below the apex there is a small notch—the “aortic notch” (fig. 94, K)—which depends on a positive wave formed in the root of the aorta, owing to the closure of the aortic valves, and propagated with almost wholly undiminished energy into the carotid artery. Quite close to this notch, if the curve be obtained with minimal friction, the first elastic vibration occurs (fig. 94, II, e). Above the middle of the descending part of the curve is the dicrotic elevation, R, produced by the reflection of a positive wave from the already closed semi-lunar valves. The dicrotic wave is relatively small on account of the high tension in the carotid artery. After this the curve falls rapidly, but in its lowest third two small elevations may be seen. Of these the former is due to elastic vibration. The latter represents a *second* dicrotic wave (fig. 94, III, R). Here there is a *true trikotism*, which is more easily obtained from the carotid on account of the shortness of the arterial channel.

2. *Axillary Artery* (fig. 94, IV). In this curve the ascent is very steep, while in the descent near the apex there is a small (aortic) elevation, K, caused by a positive wave, produced by the closure of the aortic valves. Below the middle there is a tolerably high dicrotic elevation, R, higher than in the carotid curve; because in the axillary artery the arterial tension is less, and permits a greater development of the dicrotic wave. Further on, two or three small elastic vibrations occur, e, e.

3. *Radial Artery* (fig. 94, V to X; fig. 106, R and R₁). The line of ascent (fig. 94) is tolerably high and sudden—somewhat in the form of a long f. The apex P is well marked. Below this, if the tension be high, two elastic vibrations may occur (V, e, e), but if it be low only one (VI to IX, e). About the middle of the curve is the well-marked dicrotic elevation, R. This wave is least pronounced in a small hard pulse, and when the artery is much distended (fig. 94, VII, R); it is larger when the tension is low (fig. 94, IX, R), and is greatest of all when the pulse is dicrotic (X, R). Two or three small elastic elevations occur in the lowest part of the curve.

4. Femoral Artery (fig. 94, XI, XII). The ascent is steep and high—the apex of the curve is not unfrequently broad, and in it the closure of the aortic valves (K) is indicated. The curve falls rapidly towards its lowest third. The dirotic elevation, R, occurs late after the beginning of the curve, and there are also small elastic elevations (*c, c*).

Pedal Artery (fig. 94, XIV, XV), and **Posterior Tibial** (XIII). In pulse-curves obtained from these arteries there are well-marked indications that the apparatus (heart) producing the waves is placed at a considerable distance. The ascent is oblique and low—the dirotic elevation occurs late. Two elastic vibrations (fig. 94, XIV, *e, e*) occur in the descent, but they are very close to the apex, while the elastic vibrations at the lower part of the curve are feebly marked. Fig. 102 is from the posterior tibial. When measured, it gives the following result:—

$$\left. \begin{array}{l} 1 \text{ to } 2 \quad . \quad . \quad 9.5 \\ 1 \text{ to } 3 \quad . \quad . \quad 20 \\ 1 \text{ to } 4 \quad . \quad . \quad 30.5 \\ 1 \text{ to } 6 \quad . \quad . \quad 68 \end{array} \right\} 1 \text{ vibration is } = 0.01613 \text{ sec.}$$

73. Anacrotism.—As a general rule, the line of ascent of a pulse-curve has the form of an *f*, and is nearly vertical. The arterial walls are thrown into elastic vibration by the pulse-beat, and the number of vibrations depends greatly upon the tension of the arterial walls. The distention of the artery, or what is the same thing, the ascent of the sphygmogram, usually occurs so rapidly that it is equal to *one* elastic vibration. The elongated *f* shape of the ascent is fundamentally just a prolonged elastic vibration. When the number of vibrations causing the elastic variation is small, and when the line of ascent is prolonged, two elevations occasionally occur in the line of ascent. Such a condition may occur normally (fig. 94, VIII, at 1 and 2; X, at 1 and 2). When a series of closely-placed elastic vibrations occur in the upper part of the line of ascent, so that the apex appears dentate and forms an angle with the line of ascent, then the condition becomes one of **anacrotism** (fig. 103, *a, a*), which, when it is so marked, may be characterised as pathological. Anaerotism of the pulse occurs when the time of the influx of the blood is longer than the time occupied by an elastic vibration. Hence it takes place:—

(1) In **dilatation and hypertrophy of the left ventricle**, *e.g.*, fig. 103, A, a tracing from the radial artery of a man suffering from contracted kidney, the large volume of blood expelled with each systole requires a long time to dilate the tense arteries.

(2) When the **extensibility of the arterial wall is diminished**, even the normal amount of blood expelled from the heart at every systole requires a long time to dilate the artery. This

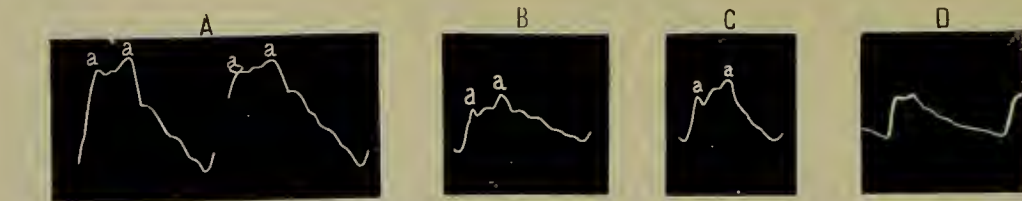


Fig. 103.

Anacrotic radial pulse-tracings. *a, a*, the anaerotic parts.

occurs in old people where the arteries tend to become rigid, *e.g.*, in atheroma. Cold also stimulates the arteries so that they become less extensile. Within one hour after a tepid bath, the pulse assumes the anaerotic form (fig. 103, D) (*G. v. Liebig*).

(3) When the blood stagnates in consequence of great diminution in the velocity of the blood-stream, as occurs in **paralysed limbs**, the volume of blood propelled into the artery at every systole no longer produces the normal distention of the arterial coats, and anaerotic notches occur (fig. 103, B).

(4) After **ligature of an artery**, when blood slowly reaches the peripheral part of the vessel through a relatively small collateral circulation, it also occurs. If the brachial artery be compressed so that the blood slowly reaches the radial, the radial pulse may become anaerotic. It often occurs in stenosis of the aorta, as the blood has difficulty in getting into the aorta (fig. 103, C).

Recurrent Pulse.—If the radial artery be compressed at the wrist, the pulse-beat reappears on the distal side of the point of pressure through the arteries of the palm of the hand (*Jaraut, Neidert*). The curve is **anacrotic**, and the dirotic wave is diminished, while the elastic elevations are increased.

(5) A special form of anacrotism occurs in cases of well-marked insufficiency of the aortic valves. Practically, in these cases, the aorta remains permanently open. The contraction of the left auricle causes in the blood a wave-motion, which is at once propagated through the open mouth of the aorta into the large blood-vessels. This wave is followed by the wave caused by the contraction of the hypertrophied left ventricle, but of course the former wave is not so large as the latter. In insufficiency of the aortic valves, the auricular wave occurs before the ventricular wave in the ascending part of the curve. The auricular is well marked only in the large vessels, for it soon becomes lost in the peripheral vessels. Fig. 104, I, was obtained from the carotid of a man suffering from *well-marked* insufficiency of the aortic valves, with considerable hypertrophy of the left ventricle and left auricle. The ascent is steep, caused by the force of the contracting heart. In the apex of the curve are two projections; A is the anacrotic auricular wave, and V is the ventricular wave. Fig 104, II, is a curve obtained from the *sub-*

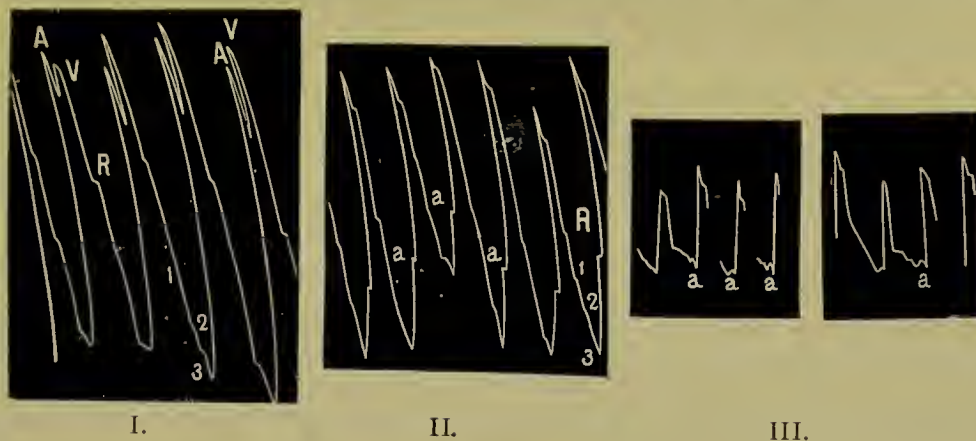


Fig. 104.

I, II, III, curves with anacrotic elevations, *a*, in insufficiency of the aortic valves.

clavian artery of the same individual. In the femoral artery the auricular projection is only obtained when the friction of the writing-style is reduced to the minimum, and when it occurs it immediately precedes the beginning of the ascent (fig. 98, III, *a*). The pulse-curve, in cases of aortic insufficiency, is also characterised by—(1) its considerable height; (2) the rapid fall of the lever from the apex of the curve, because a large part of the blood which is forced into the aorta regurgitates into the left ventricle when the ventricle relaxes; (3) not unfrequently a projection occurs at the apex, due to the elastic vibration of the tense arterial wall; (4) the dicrotic wave (R) is small compared with the size of the curve itself, because the pulse-wave, owing to the lesion of the aortic valves, has not a sufficiently large surface to be reflected from (fig. 97). The great height of the curve is explained by the large amount of blood projected into the aortic system by the greatly hypertrophied and dilated ventricle.

74. INFLUENCE OF RESPIRATION ON THE PULSE-CURVE.—The **respiratory movements** influence the pulse in two different ways—(1) in a purely **physical** way. Stated broadly, the blood-pressure is lowest at the beginning of inspiration and highest at the beginning of expiration; but when we consider the effect on the pulse-curve, it is found that it varies with the depth, rapidity, and ease of respiration; (2) the respiratory movements are accompanied by stimulation of the **vasomotor centre**, which produces variations of the blood-pressure.

1. Normal Respiration.—Fig. 105 shows what sometimes, but by no means always, happens. During **inspiration**, owing to the dilatation of the thorax, more arterial blood is retained within the chest, while at the same time venous blood is sucked into the right auricle by the aspiration of the thorax; as a consequence of this, at first the tension in the arteries must be less during inspiration. The diminution of the chest during **expiration** favours the flow in the arteries, while it retards the flow of the venous blood in the *venæ cavae*, two factors which raise the tension in the arterial system. The expiration preceding an inspiration causes less blood to flow to the heart, hence the contractions of the heart at the beginning of inspiration do not fill the aorta so full; the opposite result obtains with the

inspiration preceding the expiration. The difference of pressure explains the difference in the form of the pulse-curve obtained during inspiration and expiration, as in fig. 105 and fig. 94, I, III, IV, in which J indicates the part of the curve which occurred during inspiration, and E the expiratory portion. The following are the points of difference:—(1) The greater distention of the arteries during expiration causes all the parts of the curve occurring during this phase to

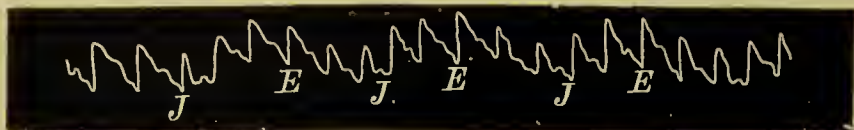


Fig. 105.

Influence of the respiration upon the pulse. J, inspiration; E, expiration.

be higher; (3) the line of ascent is lengthened during expiration, because the expiratory thoracic movement helps to increase the force of the expiratory wave; (3) owing to the increase of the pressure, the dicrotic wave must be less during expiration; (4) for the same reason the elastic elevations are more distinct and occur higher in the curve near its apex. The **frequency of the pulse** is slightly less during expiration than during inspiration.

2. This purely mechanical effect of the respiratory movements is modified by the simultaneous stimulation of the **vasomotor centre** which accompanies these movements. At the beginning of inspiration the blood-pressure in the arteries is lowest, but it begins to rise during inspiration, and increases until the end of the inspiratory act, reaching its maximum at the beginning of expiration; during the remainder of the expiration the blood-pressure falls until it reaches its lowest level again at the beginning of inspiration (compare § 85, f); the pulse-curves are similarly modified, and exhibit the signs of greater or less tension of the arteries corresponding to the phases of the respiratory movements. [There is, as it were, a displacement of the blood-pressure curve relative to the respiratory curve.]

Forced Respiration.—With regard to the effect produced on the pulse-curve by a powerful expiration and a forced inspiration, observers are by no means agreed.

Valsalva's Experiment.—Strong expiratory pressure is best produced by closing the mouth and nose, and then making a great expiratory effort (§ 60); *at first* there is increase of the blood-pressure, while the form of the pulse-waves resembles that which occurs in ordinary expiration, the dicrotic wave being less developed; but, when the forced pressure is long continued, the pulse-curves have all the signs of diminished tension. This effect is due to the action of the vasomotor centre, which is affected reflexly from the pulmonary nerves. We must assume that forced expiration, such as occurs in Valsalva's experiment, acts by *depressing* the activity of the vasomotor centre (§ 371, II.). Coughing, singing, and declaiming act like Valsalva's experiment, while the frequency of the pulse is increased at the same time. *After* the cessation of Valsalva's experiment, the blood-pressure *rises* above the normal state (*Sommerbrodt*) almost as much as it fell below it, the normal condition being restored within a few minutes (*Lenzmann*).

Müller's Experiment.—When the thorax is in the expiratory phase, close the mouth and nose, and take a deep inspiration so as forcibly to expand the chest (§ 60). At first the pulse-curves have the characteristic signs of diminished tension, viz., a higher and more distinct dicrotic wave; then the tension can, by nervous influences, be increased, just as in fig. 106, where C and R are tracings taken from the carotid and radial arteries respectively, during Müller's experiment, in which the dicrotic waves *r*, *r*, indicate the diminished tension in the vessels. In C₁ and R₁, taken from the same person during Valsalva's experiment, the opposite condition occurs.

Compressed Air.—On *expiring* into a vessel resembling a spirometer (see Respiration), (Waldenburg's respiration apparatus), and filled with compressed air, the same result is obtained as in Valsalva's experiment—the blood-pressure falls and the pulse-beats increase; conversely the *inspiration* from this apparatus of air under less pressure acts like Müller's experiment, *i.e.*, it increases the effect of the inspiration, and afterwards increases the blood-pressure, which may either remain increased on continuing the experiment, or may fall (*Lenzmann*).

The *inspiration* of compressed air diminishes the mean blood-pressure (*Zuntz*), and the after-effect continues for some time. The pulse is more frequent both during and after the experi-

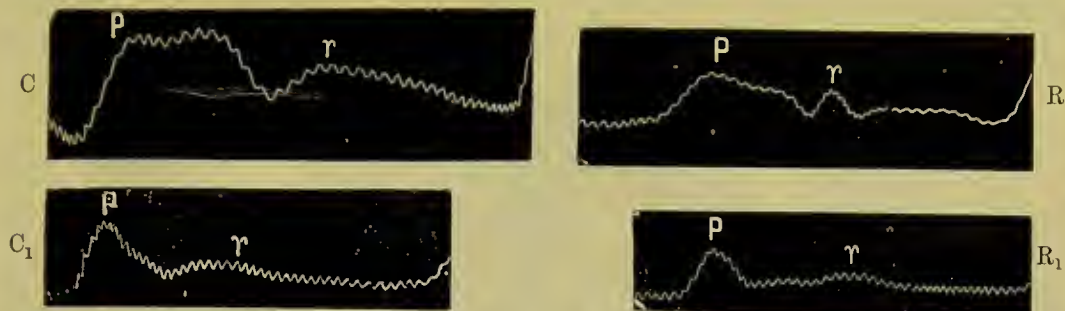


Fig. 106.

C, curve from the carotid, and R, radial, during Müller's experiment; C₁ and R₁ during Valsalva's experiment. Curves written on a vibrating surface.

ment. *Expiration* in rarefied air increases the blood-pressure. The effects which depend upon the action of the nervous system do not occur to the same extent in all cases. Exposure to compressed air in a pneumatic cabinet lowers the pulse-curve, the elastic vibrations become indistinct, and the dirotic wave diminishes and may disappear (*v. Vivenot*). The heart's beat is slowed, and the blood-pressure raised (*Bert*). Exposure to rarefied air causes the opposite result, which is a sign of diminished arterial tension.

Pulsus Paradoxus.—Under pathological conditions, especially when there is union of the heart or its large vessels with the surrounding parts, the pulse during inspiration may be

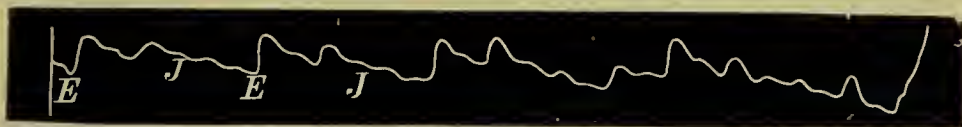


Fig. 107.

Pulsus paradoxus (after *Kussmaul*). E, expiration; J, inspiration.

extremely small and changed, or may even be absent, while it is increased in expiration (fig. 107). This condition has been called **pulsus paradoxus** (*Griesinger, Kussmaul*). It depends upon a diminution of the arterial lumen during the inspiratory movement [as in contraction of the air-passages, and in cases of pericardial adhesions]. Even in health it is possible by a change of the inspiratory movement to produce the p. paradoxus (*Riegel, Sommerbrodt*).

75. INFLUENCE OF PRESSURE ON THE PULSE-CURVE.—It is most important to know the actual pressure which is applied to an artery while a sphygmogram is being taken. The changes affect the *form* of the curve as well as the relation of individual parts thereof. In fig. 108, *a, b, c, d, e* are radial curves; *a* was taken with minimal pressure, *b* with 100, *c*, 200, *d* 250, and *e* 450 grams pressure, while A, B, C, D show the relations as to the time of occurrence of the individual phenomena where the weight was successively increased. The study of these curves yields the following results:—(1) When the weight is small, the dirotic wave is relatively less; the whole curve is high; (2) with a moderate weight (100 to 200 grams) the dirotic wave is best marked, the whole curve is somewhat lower; (3) on increasing the weight the size of the dirotic wave again diminishes; (4) the fine elastic vibrations preceding the dirotic wave appear first when a weight of 220 to 300 grams is used; (5) the rapidity of the pulse changes with increasing weight, the time occupied by the ascent becoming shorter, the descent becoming longer; (6) the height of the entire curve decreases as the weight increases. In every sphygmogram the pressure under which it was obtained ought always to be stated. In fig. 108, A, B, are curves obtained from the radial artery of a healthy student. The pressure exerted upon the artery for A was 100; B, 220 grms. (1 vibration = 0.01613 sec.).

If pressure be exerted upon an artery for a long time, the strength of the pulse is gradually increased. If, after subjecting an artery to considerable pressure, a lighter weight be used, not unfrequently the pulse-curve assumes the form of a dirotic pulse, owing to the greater develop-

ment of the dirotic elevation. When strong pressure is applied, the blood is forced to find its way through collateral channels. When the chief artery ceases to be compressed, the total area is, of course, considerably and suddenly enlarged, which results in the production of a dirotic elevation. Fig. 94, X, is such a dirotic curve obtained after considerable pressure had been applied to the artery.

76. TRANSMISSION OF PULSE-WAVES.—The pulse-wave proceeds throughout the arterial system from the root of the aorta, so that the pulse is felt sooner in parts lying near the heart than in the peripheral arteries. E. H. Weber calculated

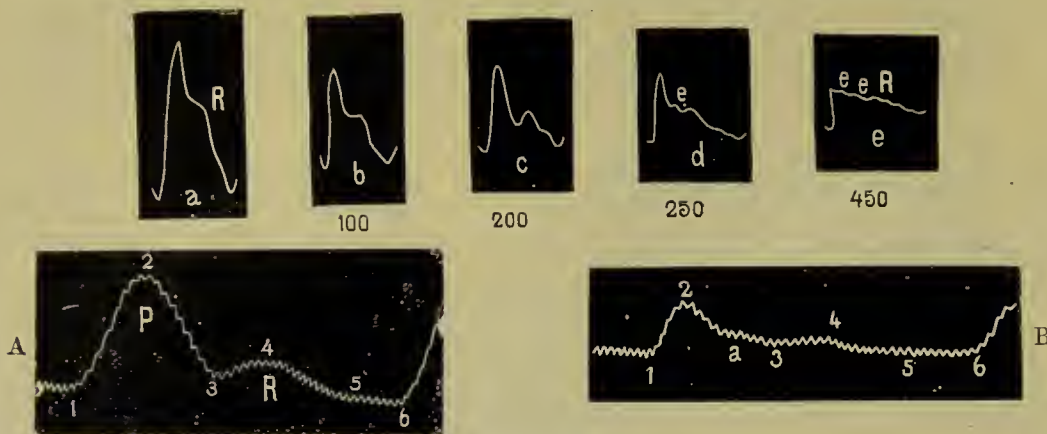


Fig. 108.

Various forms of curves (radial) obtained by gradually increasing the pressure.

ated the **velocity of the pulse-wave** as 9.240 metres [$28\frac{1}{2}$ feet] per second, from the difference in time between the pulse in the external maxillary artery and the dorsal artery of the foot. Czermak showed that the elasticity was not equal in all the arteries, so that the velocity of the pulse-wave cannot be the same in all. The pulse-wave is propagated more slowly in the arteries with soft extensile walls than in arteries with resistant and thick walls, so that it is transmitted more rapidly in the arteries of the lower extremities than in those of the upper. It is still slower in children.

77. PULSE-WAVE IN ELASTIC TUBES.—Waves similar to the pulse may be produced in elastic tubes. (1) According to E. H. Weber the velocity of propagation of the waves is 11.205 metres per sec.; according to Donders, 11–13 metres (34–42 feet). (2) According to E. H. Weber increased internal tension causes only an inconsiderable decrease; Rive found a great decrease; Donders found no obvious difference; while Marey found an increased velocity. (3) Donders found the velocity to be the same in tubes 2 mm. in diameter as in wider tubes, but Marey believes that the velocity varies when the diameter of the tube changes. (4) The velocity is less, the smaller the elastic coefficient. (5) The velocity increases with increased thickness of the wall, while it diminishes when the specific gravity of the fluid increases.

Moens has recently formulated the following laws as to the velocity of propagation of waves in elastic tubes:—(1) It is inversely proportional to the square root of the specific gravity of the fluid; (2) it is as the square root of the thickness of the wall, the lateral pressure being the same; (3) it is inversely as the square root of the diameter of the tube, the lateral pressure being the same; (4) it is as the square root of the elastic coefficient of the wall of the tube, the lateral pressure being the same (*Valentin*).

(A) The velocity of the wave is 11.809 metres per second.

(B) The *intra-vascular pressure* has a decided influence on the velocity; thus, in the tube, A, with 18 cm. (Hg) pressure, the velocity per metre = 0.093 second, while with 21 cm. pressure (Hg) = 0.095 second per metre.

(C) The *specific gravity of the liquid* influences the velocity of the pulse-wave. In *mercury* the wave is propagated four times more slowly than in water.

(D) The velocity in a tube which is more rigid and not so extensile is greater than in a tube which is easily distended.

78. VELOCITY OF THE PULSE-WAVE IN MAN.—Landois obtained the following results in a student:—Difference between carotid and radial = 0.074 second (the distance being taken

as 62 centimetres); carotid and femoral = 0.068 second; femoral (inguinal region) and posterior tibial = 0.097 second (distance estimated at 91 centimetres). [Waller obtained between the heart and carotid 0.10 second; heart and femoral, 0.18 sec.; heart and dorsalis pedis, 0.22.]

The **velocity of the pulse-wave** in the arteries of the upper extremities = 8.43 metres per second, and in those of the lower extremity 9.40 metres per second, [*i.e.*, about 30 feet per second]. The velocity is greater in the less extensible arteries of the lower extremities than in those of the upper limb. For the same reason it is less in the peripheral arteries and in the yielding arteries of children (*Czermak*).

E. H. Weber estimated the velocity at 9.24 metres per second; Garrod, 9-10.8 metres; Grashey, 8.5 metres; Moens, 8.3 metres, and with diminished pressure during Valsalva's experiment 7.3 metres (§ 60, § 74).

Influencing Conditions.—In animals, hæmorrhage, slowing of the heart produced by stimulation of the vagus (*Moens*), section of the spinal cord, deep morphia-narcosis, and dilatation of the blood-vessels by heat, produce *slowing* of the velocity, while stimulation of the spinal cord *accelerates* it (*Grunmach*).

The **wave-length of the pulse-wave** is obtained by multiplying the duration of the inflow of blood into the aorta = 0.08 to 0.09 second (§ 51), by the velocity of the pulse-wave.

Method.—Place the knobs of two tambours (fig. 88) upon the two arteries to be investigated, or place one over the apex-beat and the other upon an artery. These receiving tambours are connected with two registering tambours, as in Brondgeest's pansphygmograph (§ 67, fig. 88), so that their writing-levers are directly over each other, and so arranged as to write simultaneously on *one* vibrating plate attached to a tuning-fork. [Or they may be made to write upon a revolving cylinder, whose rate of movement is ascertained by causing a tuning-fork of a known rate of vibration to write under them.] The apparatus is improved by using rigid tubes and filling them with water, in which all impulses are rapidly communicated. In arteries which are

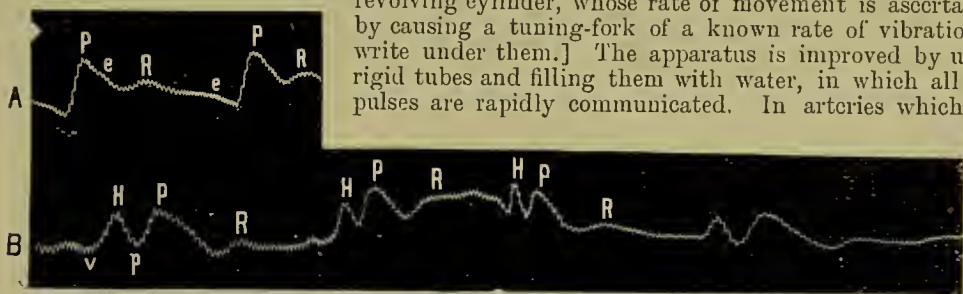


Fig. 109.

A, curve of radial artery on a vibrating surface (1 vib. = 0.01613 sec.); P, apex of curve; e, e, elastic vibrations; R, dicrotic wave. B, curve of same radial taken along with the heart-beat; v, H, P, contraction of the ventricle.

distant from each other, or in the case of the heart and an artery, the two knobs of the receiving tambours may be connected by means of a Y-tube with *one* writing-lever. In fig. 109, B is a curve from the radial artery taken in this way. In it v H P indicates contraction of the ventricle; H, the apex of the ventricular contraction; P, the primary apex of the radial curve; v, the beginning of the ventricular contraction; p, of the radial pulse. A is the curve of the radial artery alone. From these curves it is evident that in this instance nine vibrations occur between the beginning of the ventricular contraction and the beginning of the pulse in the radial artery = 0.15 sec.

In fig. 110 the difference between the carotid and the posterior tibial pulse = 0.137 sec.

Pathological.—In cases of *diminished extensibility* of the arteries, *e.g.*, in athleroma (§ 77, D), the pulse-wave is propagated more rapidly. Local dilatations of the arteries, as in **aneurisms**, cause a retardation of the wave, and a similar result arises from local constrictions. Relaxation of the walls of the vessels in high fever retards the movement (*Hamernijk*).

79. OTHER PULSATILE PHENOMENA.—1. In the mouth and nose, when they are filled with air, and the glottis closed, pulsatile phenomena (due to the arteries in their soft parts), may be found communicating a movement to the contained air. The curves obtained are relatively small, and closely resemble the curve of the carotid. A similar pulse is obtained in the **tympanum** with intact membrana tympani, and when the soft parts of the tympanum are congested (*Schwartz*, *Tröltsch*).

2. **Entoptical Pulse.**—After violent exercise, an illumination, corresponding to each pulse-beat, occurs on a dark optical field. When the optical field is bright, an analogous darkening occurs. The ophthalmoscope occasionally reveals pulsation of the retinal arteries (*Jäger*), which becomes marked in insufficiency of the aortic valves.

3. **Pulsatile Muscular Contraction.**—The *orbicularis palpebrarum* muscle contracts under similar conditions synchronously with the pulse; and it is perhaps due to the pulse-beat exciting the sensory nerves reflexly. The Brothers Weber found that not unfrequently, while walking, the step and pulse gradually and involuntarily coincide.

4. When the legs are crossed as one sits in a chair, the leg which is supported is raised with each pulse-beat, and it gives also a second or dirotic elevation.

5. If, while a person is quite quiet, the incisor teeth of the lower jaw be made just to touch



Fig. 110.

Curves of the carotid and posterior tibial taken simultaneously with Brondgeest's pansphygmograph writing upon a vibrating-plate attached to a tuning-fork. The arrows indicate the identical moment of time in each curve.

the upper incisors very lightly, we detect a double beat of the lower against the upper teeth, owing to the pulse-beat in the external maxillary artery raising the lower jaw. The second elevation is due to the closure of the semi-lunar valves, and not to a dirotic wave.

6. **Brain and Fontanelles.**—The large arteries at the base of the *brain* communicate a movement to it, while similar movements occur with respiration—rising during expiration and falling during inspiration. These movements are visible in the *fontanelles of infants*. The respiratory movements depend upon variations in the amount of blood in the veins of the cranial cavity, and also upon the respiratory variations of the blood-pressure.

7. Amongst **pathological** phenomena are (a) the beating in the epigastrium, *e.g.*, in hypertrophy of the right or left ventricle, caused, it may be, by deep insertion of the diaphragm, and it may be, partly, by the beating of a dilated abdominal aorta or celiac axis.

(b) **Aneurisms** or *abnormal dilatations* of the arteries cause an abnormal pulsation, while they produce a *slowing in the velocity of the pulse-wave* in the corresponding artery. Hence the pulse appears later in such an artery than in the artery on the healthy side. *Hypertrophy and dilatation of the left ventricle* cause the arteries near the heart to pulsate strongly. In the analogous condition of the right ventricle, the beat of the pulmonary artery may be seen and felt in the second left intercostal space.

80. **VIBRATIONS OF THE BODY DUE TO THE HEART.**—The beating of the heart and large arteries communicates compound vibrations to the body as a whole. If a person be placed

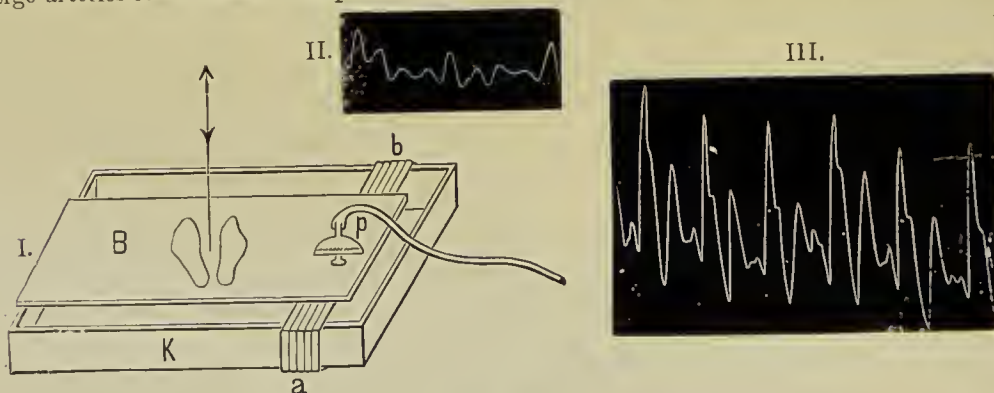


Fig. 111.

- I. Elastic support for registering the molar motions of the body—K, wooden box; B, feet of patient; p, eardiograph; a, b, elastic tubing. II. Vibration curves of a healthy person. III. Curve obtained from a patient with insufficiency of the aortic valves and great hypertrophy of the heart.

in an erect attitude in the scale-pan of a large balance, the index oscillates, and its movements coincide with the heart's movements (*Gordon*).

Method.—Take a long four-sided box, K, open at the top, and arrange several coils, *a*, *b*, of stout caoutchouc tubing round one end (fig. 111). A wooden board, B, is so placed that it rests with one end on the caoutchouc tubing, and with the other on the narrow end of the box. The person to be experimented upon, A, stands vertically and firmly on this board. A receiving tambour, *p*, is placed against the surface of the board next the elastic tube, which registers the vibrations of the foot-support. Fig. III. is a curve showing such vibrations, each heart-beat being followed in this case by four oscillations. To ascertain the relations and causes of these vibrations, it is necessary to obtain, simultaneously, a tracing of the heart and the vibratory curve. For this purpose use the two tambours of Brondgeest's pansphygmograph (§ 67, 76), placing one knob or pad over the heart and the other on the foot-support, and allow the writing-tambours to inscribe their vibrations on a glass plate attached to a tuning-fork (Gordon).

In the *lower or cardiac impulse curve* (fig. 111), the rapidly-rising part is due to the ventricular systole. It contains eight vibrations (1 vib. = 0.01613 sec.). The beginning of the ventricular systole is indicated in the fig. by -36, -3, -17.

If the corresponding numbers in the upper or *vibratory curve* are studied, it is obvious that at the moment of ventricular systole the body makes a downward vibration, i.e., it exercises greater pressure upon the foot-support. Gordon interprets his curve as giving exactly the opposite

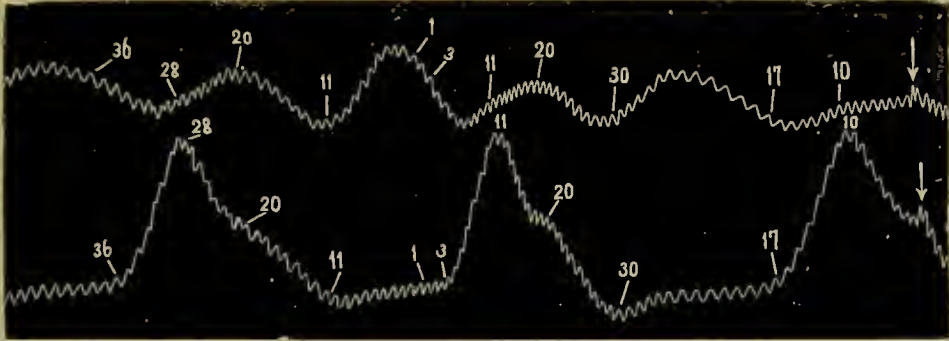


Fig. 112.

The upper curve is the vibration-curve of a healthy person, and the lower one a tracing of the apex-beat.

result. This downward motion, however, lasted only during five vibrations of the tuning-fork; during the last three vibrations, corresponding to the systole, there is an ascent of the body corresponding to a less pressure upon the foot-plate. When the ventricle empties itself, it undergoes a movement in a downward and outward direction—Gutbrodt's "reaction impulse."

In the *upper curve* analogous numbers are employed to indicate the vibrations occurring simultaneously, viz., -28, -11, -10. The closure of the semi-lunar valves is well marked in the three heart-beats at 20, -20. This closure is indicated in analogous points in both curves, after which there is a descent of the foot-support, and this corresponds to the downward propagation of the pulse-wave through the aorta to the vessels of the feet.

Pathological.—In insufficiency of the aortic valves as shown in fig. 111, III., the vibration communicated to the body is very considerable.

81. THE BLOOD CURRENT.—Cause.—The closed and much-branched **vascular system**, whose walls are endowed with elasticity and contractility, is not only completely filled with blood, but it is **over-filled**. The total volume of the blood is somewhat greater than the capacity of the entire vascular system. Hence it follows that the mass of blood must exert **pressure** on the walls of the entire system, thus causing a corresponding dilatation of the elastic vascular walls (Brunner). This occurs only during life; after death the muscles of the vessels relax, and fluid passes into the tissues, so that the blood-vessels come to contain less fluid, and some of them may be empty.

If the blood were uniformly distributed throughout the vascular system, and under the same pressure, it would remain in a position of equilibrium (as after death). If, however, the pressure be raised in one section of the tube, the blood will move from the part where the pressure is higher to where it is lower; so that the **blood-current is a result of the difference of pressure** within the vascular system. If either the aorta or the venæ cavæ be suddenly ligatured in a living

animal, the blood continues to flow, but gradually more slowly, until the difference of pressure is equalised throughout the entire vascular system.

The **velocity** of the current will be greater the greater the difference of pressure, and the less the resistance opposed to the blood-stream.

The **difference of pressure which causes the current is produced by the heart**. Both in the systemic and pulmonary circulation the point of greatest pressure is in the root or beginning of the arterial system, while the point of lowest pressure is in the terminal portion of the venous orifices at the heart. Hence the blood flows continually from the arteries through the capillaries into the venous trunks. The heart keeps up the difference of pressure required to produce this result; with each systole of the ventricles a certain quantity of blood is forced into the beginning of the arteries, while at the same time an equal amount flows from the venous orifices into the auricles during their diastole (*E. H. Weber*).

Donders showed that the action of the heart not only causes the difference of pressure necessary to establish a blood-current, but also **raises the mean pressure** within the vascular system. The terminations of the veins at the heart are wider and more extensible than the arteries where they arise from the heart. As the heart propels a volume of blood into the arteries equal to that which it receives from the veins, it follows that the arterial pressure must rise more rapidly than the venous pressure diminishes, since the arteries are not so wide nor so extensible as the veins. Thus the total pressure must also increase.

Cause of Continuous Flow.—The volume of blood expelled from the ventricles at every systole would give rise to a *jerk* or intermittent movement of the blood-stream—(1) if the tubes had rigid walls, as in such tubes any pressure exerted upon their contents is propagated momentarily throughout the length of the tube, and the motion of the fluid ceases when the propelling force ceases; (2) the flow would also be intermittent in character in elastic tubes if the time between two successive systoles were longer than the duration of the current necessary for the compensation of the difference of pressure caused by the systole. If the time between two successive systoles be shorter than the time necessary to equilibrate the pressure, the current will become **continuous**, provided the resistance at the periphery of the tube be sufficiently great to bring the elasticity of the tube into action. The more rapidly systole follows systole, the greater the difference of pressure becomes, and the more distended the elastic walls. Although the current thus produced is continuous, a sudden rise of pressure is caused by the forcing in of a mass of blood at every systole, so that with every systole there is a sudden jerk and *acceleration of the blood-stream* corresponding to the pulse (compare § 64).

This sudden jerk-like acceleration of the blood-current is propagated throughout the arterial system with the velocity of the pulse-wave; both phenomena are due to the same fundamental cause. Every pulse-beat causes a temporary rapid progressive acceleration of the particles of the fluid. But just as the form-movement of the pulse is not a simple movement, neither is the pulsatile acceleration a simple acceleration. It follows the course of the development of the pulse-wave. The pulse-curve is the graphic representation of the pulsatory acceleration of the blood-stream. Every rise in the curve corresponds to an acceleration, every depression to a retardation of the current.

[**Method: Rigid and Elastic Tubes.**—These facts are easily demonstrated. Tie a Higginson's syringe to a piece of gas-pipe. On forcing water through the **rigid tube**, by compressing the pump, the water will flow out at the other end of the tube in jets, while during the intervals of pulsation no water will flow out. As the walls of the tube are rigid, just as much fluid flows out as is forced into the tube. If a similar arrangement be made, and a long **elastic tube** be used, a **continuous outflow** is obtained, provided the pulsations occur with sufficient rapidity and the length of the tube, or the resistance at its periphery, be sufficient to bring the elasticity of the tube into action. This can be done by putting a narrow cannula in the outflow end of

the tube, or by placing a clamp on it so as to diminish the exit aperture. This apparatus converts the intermittent flow into a continuous current.] The fire-engine is a good example of the conversion of an intermittent inflow into a uniform outflow. The air in the reservoir is in a state of elastic tension, and it represents the elasticity of the vascular walls. When the pump is worked slowly, the outflow of the water occurs in jets, and is interrupted. If the pumping movement be sufficiently rapid, the compressed air in the reservoir causes a continuous outflow, which is distinctly accelerated at every movement of the pump. [The ordinary spray-producer is another good example.]

[Thus, there are two factors—a **central** one, the **heart**,—and a **peripheral** one, the amount of **resistance** especially in the arterioles. Either or both may be varied, and as this is done, so will the pressure and velocity vary.]

Current in the Capillaries.—In the **capillaries** the pulsatile acceleration of the current ceases with the extinction of the pulse-wave. The great resistance which is offered to the current towards the capillary area causes both to disappear. It is only when the capillaries are greatly dilated, and when the arterial blood-pressure is high, that the pulse is propagated through the capillaries into the beginning of the veins. A **venous pulse** is observed in the veins of the sub-maxillary gland after stimulation of the chorda tympani nerve, which contains the vaso-dilator nerves for the blood-vessels of this gland. If the finger be constricted with an elastic band, so as to hinder the return of the venous blood, and to increase the arterial blood-pressure, while at the same time dilating the capillaries, an intermittent increased redness occurs, which corresponds with the well-known throbbing sensation in the swollen finger. This is due to the **capillary pulse**. [Roy and Graham Brown found that pulsatile phenomena were produced in the capillaries by increasing the extra-vascular pressure (§ 86). Quincke called attention to the capillary pulse, which can often be seen under the finger-nails. Extend the fingers completely, when a whitish area appears under the nails. A red area near the free margin of the nail advances and retires with each pulse-beat. It is well marked in some diseased conditions of the heart, especially in incompetence of the aortic valves, and is probably produced by increased extra-vascular pressure. If the finger be drawn over the skin, *e.g.*, of the forehead, in such a person the alternate flushing and paling due to the capillary pulse is readily observed.]

82. SCHEMATA OF THE CIRCULATION.—E. H. Weber constructed a scheme of the circulation. It consisted of a force-pump with properly arranged valves to represent the heart, portions of gut for the arteries and veins, and a piece of glass tubing containing a piece of sponge to represent the capillaries. Various schemes have been invented, including the very complicated one of Marey, [the extremely ingenious one of v. Thanhofer, and the thoroughly practical one of Rutherford].

83. CAPACITY OF THE VENTRICLES.—Since the right and left ventricles contract simultaneously, and just the same volume of blood passes through the pulmonary as through the systemic circulation, it follows that the right ventricle must be just as capacious as the left. The capacity of the ventricles has been estimated in the following ways :—

Methods.—(1) **Directly**, by filling the *dead* relaxed ventricle with blood or an injection mass. This method is unsatisfactory and inaccurate.

(2) **Indirectly**, Volkmann (1850) estimated it thus :—Estimate the sectional area of the aorta, and the velocity of the blood-stream in it (§ 91). From this calculate the amount of blood passing through the aorta in the unit of time. As the total quantity of blood in the body is known ($=\frac{1}{15}$ of the body-weight), we can easily calculate how long this takes to flow through the aorta. We must also know the number of beats during the time of the circulation. From these data, and from experiments on animals, Volkmann estimated the volume of blood discharged at each systole by the ventricle to be $\frac{1}{100}$ of the body-weight. For a man weighing 75 kilos. this is 187.5 grams. This estimate still leaves much to be desired.

Place calculates it in the following manner :—A man uses about 500 litres of O in 24 hours. To absorb this into the venous blood (which contains about 7 vols. per cent. less O than arterial). about 7000 litres of blood must pass through the lungs in 24 hours. If one calculates 100,000 heart-beats in 24 hours, then at each systole only 70 cubic centimetres are discharged.

[**Capacity of the pulmonary and systemic circulation.**—Taking the quantity of blood in an average adult as equal to $5\frac{1}{2}$ litres, according to Jolyet and Tanziac the ratio is 2 : 11, *i.e.*, 1 litre in the pulmonary and $4\frac{1}{2}$ in the systemic circuit. This estimate for the pulmonary circuit is somewhat too low. As to the relative quantity of blood in the arterial and venous tubes as a whole, the ratio is about 1 to 2.]

84. ESTIMATION OF THE BLOOD-PRESSURE.—(A) **In Animals:** (1) **Method of Hales.**—The Rev. Stephen Hales (1727) was the first to introduce a long glass tube into a blood-vessel in order to estimate the blood-pressure by measuring the height of the column of blood.

The tube was provided at its lower end with a copper tube bent at a right angle. [The tube he used was one-sixth of an inch bore and about 9 feet long, and was inserted into the femoral

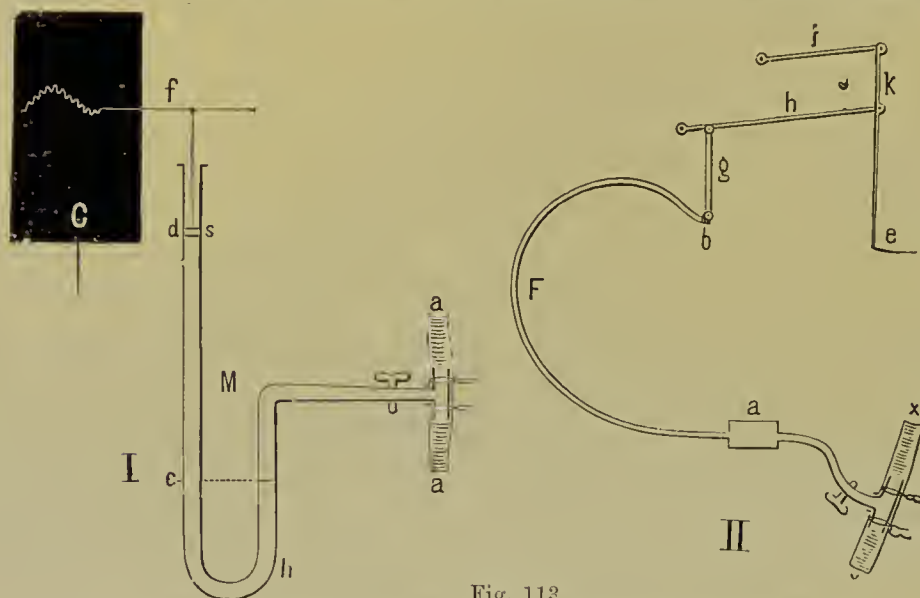


Fig. 113.

I. Scheme of C. Ludwig's kymograph. II. Fick's spring-kymograph.

artery of a horse. The height to which the blood rose in the tube was noted, as well as the oscillations of the blood that occurred with every pulsation. From the height of the column of fluid he calculated the force of the heart.]

(2) **The Hæmadynamometer of Poiseuille (1828).**—This observer used a U-shaped tube partially filled with mercury—a gauge or manometer—which was brought into connection with a blood-vessel by means of a rigid tube. [The mercury oscillated with every pulsation, and the extent of the oscillations was read off on a scale attached to the bent tube. He called the instrument a *hæmadynamometer*.]

[(3) **Vierordt** used a tube 5 or 6 feet long, and filled it with a solution of sodium carbonate, thus preventing much blood from entering the tube, while at the same time the soda solution prevented the coagulation of the blood.]

(4) **C. Ludwig's Kymograph.**—C. Ludwig employed a U-shaped manometer, but he placed a light float upon the surface of the mercury in the open limb of the tube (fig. 113, I., *d*, *s*). A writing-stylus, *f*, placed transversely on the free end of the float, inscribed the movements of the float—and, therefore, of the mercury—upon a cylinder, *c*, caused to revolve at a uniform rate. This apparatus registered the height of the blood-pressure, as well as the pulsatile and other oscillations occurring in the mercury. Volkmann called this instrument a **kymograph** or "wave-writer." The difference of the height of the column of mercury, *c*, *d*, in both limbs of the tube indicates the pressure within the vessel. If the height of the column of mercury be multiplied by 13.5, this gives the height of the corresponding column of blood. Setschenow placed a stop-cock in the lower bend, *h*, of the tube. If this be closed so as just to permit a small aperture of communication to remain, the pulsatile vibrations no longer appear, and the apparatus indi-

cates the *mean pressure*. By the term *mean pressure* is meant the limit of pressure, above and below which the oscillations occurring in an ordinary blood-pressure-tracing range. [Briefly, it is the *average* elevation of the mercurial column.]

In a **blood-pressure-tracing**, such as fig. 115, each of the **smaller waves** corresponds to a **heart-beat**, the ascent corresponds to the systole, and the descent to the diastole. The **large undulations** are due to the **respiratory movements**. It is clear that the heart-beat is expressed as a simple rise and fall (fig. 115), so that the curve of the heart-beat obtained with a mercurial kymograph differs from a sphygmographic curve.

[**Faults of a Mercurial Manometer.**—A perfect recording instrument ought to indicate the height of the blood-pressure, and also the size, form, and duration of any wave-motion communicated to it. The mercurial manometer does not give the true form of the pulse-wave, as the mercury, when once set in motion, executes vibrations of its own, owing to its great inertia, and thus the finer movements of the pulse-wave are lost. Hence a mercurial kymograph is used for registering the blood-pressure, and not for obtaining the *exact* form of the pulse-wave. Instruments with less inertia, and with no vibrations peculiar to themselves, are required for this purpose.]

[**Method of measuring the Blood-Pressure.**

—Expose the carotid of a chloralised rabbit, and isolate a portion of the vessel between two ligatures. Make an oblique slit in the artery, and into it tie a straight glass **cannula**, directing the pointed end of the cannula towards the heart. Fill the cannula with a saturated solution of sodium carbonate, taking care that no air-bubbles enter, and connect it with the **lead tube** which goes to the ascending limb of the manometer.

The tube which connects the artery with the manometer must be flexible and yet inelastic, and a lead tube is best. It is usual to connect a **pressure-bottle**, containing a saturated solution of sodium carbonate, by means of an elastic tube, with the tube attached to the manometer. This bottle can be raised or lowered. Before beginning the experiment, raise the pressure-bottle until there is a *positive* pressure of mercury in the manometer about equal to the estimated blood-pressure, and then clamp the tube of the pressure-bottle where it joins the lead tube. This positive pressure prevents the escape of blood from the artery into the solution of sodium carbonate. When all is ready, the ligature on the *cardiac* side of the cannula is removed, and immediately the float begins to oscillate and inscribe its movements upon the recording surface. The fluid within the artery exerts pressure latterly upon the sodium carbonate solution, and this in turn transmits it to the mercury. Albumoses, when injected into the blood, keep it from coagulating (p. 36). Roy finds that oil may take the place of sodic carbonate.]

[**Precautions.**—In taking a blood-pressure-tracing, after seeing that the apparatus is perfect, care must be taken that the animal is perfectly quiescent, as every movement causes a rise of blood-pressure. This may be secured by giving curare and keeping up artificial respiration, or by the carefully regulated inhalation of ether. When a drug is to be injected to test its action, if it be introduced into the jugular vein it is apt to affect the heart directly. This may be avoided by injecting it into a vein of the leg, or under the skin. The solution of the drug must not contain particles which will block up the capillaries. Care should also be taken that the carbonate of soda does not flow back into the artery.]

[**Continuous Tracing.**—When we have occasion to take a tracing for any length of time, it must be written upon a strip of paper which is moved at a uniform rate in front of the writing-

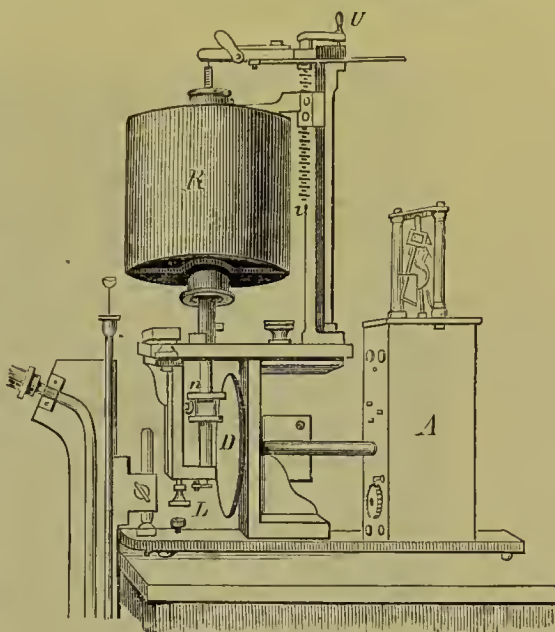


Fig. 114.

Ludwig's improved revolving cylinder, *R*, moved by the clock-work in the box *A*, and regulated by a Foucault's regulator placed on the top of the box. The disc, *D*, moved by the clock-work, presses upon the wheel, *n*, which can be raised or lowered by the screw, *L*, thus altering the position of *n* on *D*, so as to cause the cylinder to rotate at different rates. The cylinder itself can be raised by turning the handle, *U*. On the left side of the figure is a mercurial manometer. When the cylinder is used, it is covered with smoked smooth paper.

style on the float (fig. 113). Various arrangements are employed for this purpose, but it is usual to cause a cylinder to revolve, so as to unfold a roll of paper placed on a movable bobbin. As the cylinder revolves, it gradually winds off the strip of paper, which is kept applied to the revolving surface by ivory friction-wheels. In Hering's complicated kymograph a long strip of smoked paper is used. The writing-style may consist of a sable brush, or a fine glass pen filled with aniline blue dissolved in water, to which a little alcohol and glycerin are added.]

[In order to measure the height of the pressure, we must know the position of the abscissa

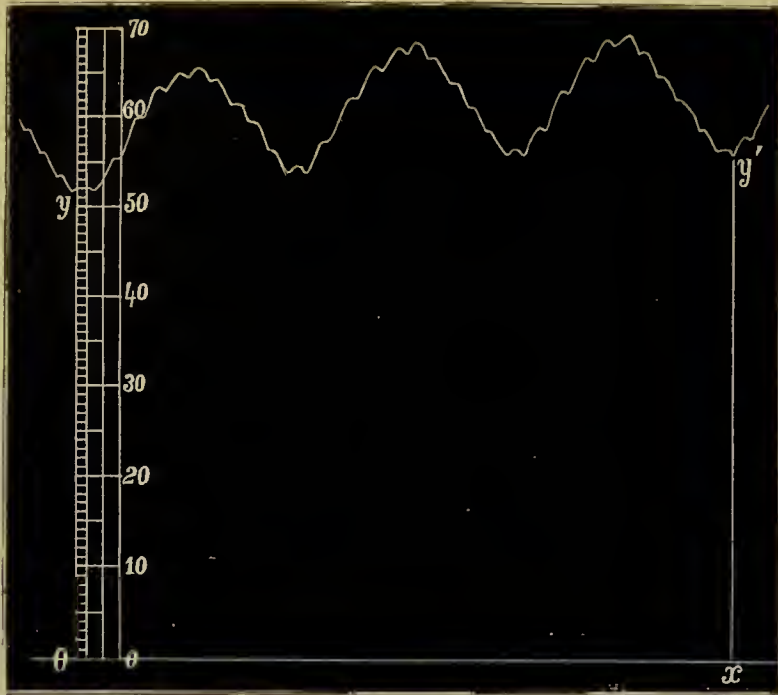


Fig. 115.

Blood-pressure curve of the carotid of a dog obtained with a mercurial manometer. $0-x$ = line of no pressure, zero line, or abscissa; $y-y'$ is the blood-pressure-tracing with small waves, each one caused by a heart-beat, and the large waves due to the respiration. A millimetre scale shows the height of the pressure in millimetres of mercury.

or line of no pressure, and it may be recorded at the same time as the blood-pressure, or afterwards. In fig. 115 $0-x$ is the zero-line or the abscissa, and the height of the vertical lines or **ordinates** may be measured by the millimetre scale on the left of the figure. The height of the blood-pressure is obtained by drawing ordinates from the curve to the abscissa, measuring their length, and multiplying by two.]

(5) **Spring Kymograph.**—A. Fick (1864) uses a hollow spring-kymograph on the principle of Bourdon's manometer (fig. 113, II).

A hollow C-shaped metallic spring, F , is filled with alcohol. One end of the hollow spring is closed, and the other end, covered by a membrane, is brought into connection with a blood-vessel by a junction piece filled with a solution of sodium carbonate. As soon as the communication with the artery is opened, the pressure rises, and the spring, of course, tends to straighten itself. To the closed end, b , there is fixed a vertical rod attached to a series of levers, h, i, k, e , one of which writes its movements upon a surface moving at a uniform rate. The blood-pressure and the periodic variations of the pulse are both recorded, although the latter is not done with absolute accuracy.

[Hering improved Fick's instrument (fig. 116). The hollow spring filled with alcohol communicates at a with the lead tube, d , passing to the cannula in the artery. To c is attached a series of light wooden levers with a writing-style, s . The lower part of d dips into a vessel, e , filled with oil or glycerin, which serves to damp the vibrations of the levers. At f is a syringe communicating with the tube, d , filled with a solution of sodic carbonate, and used for regulating the amount of fluid in the tube connecting the manometer with the blood-vessel. The whole apparatus can be raised or lowered on the toothed rod, h , by means of the millhead opposite, g , to which all the parts of the apparatus are attached.]

(6) **Fick's Flat Spring-Kymograph.**—The narrow tube, *a*, *a* (1 mm. diam.) is placed in connection with a blood-vessel by means of the cannula, *c*, and over its vertical expanded end, *A*, is fixed a caoutchouc membrane, with a projecting point, *s*, which presses against a horizontal spring, *F*, joined to a writing-lever, *H*, by an intermediate piece, *b*. The whole is held in the metallic frame, *R R* (fig. 117). In order to estimate the absolute pressure, the instrument must be compared previously with a mercurial manometer.

(B) **In man** the blood-pressure may be estimated by means of—(1) a properly **graduated sphygmograph** (§ 67). The pressure required to abolish the movement of the lever indicates approximately the vascular tension. The mean blood-pressure in the radial artery is equal to 550 grams.

(2) **Sphygmomanometer of v. Basch.**—A capsule containing fluid was placed upon a pulsating artery, while the capsule itself communicated with a mercurial manometer.

As soon as the pressure within the manometer *slightly exceeded* that within the artery, the artery was compressed so that a sphygmograph placed on a peripheral portion of the vessel ceased to beat. Both arrangements do not give the exact pressure within the artery; they only indicate the pressure which is required to compress the artery and the overlying soft parts. The pressure required to compress the walls of an empty artery, however, is very small compared with the

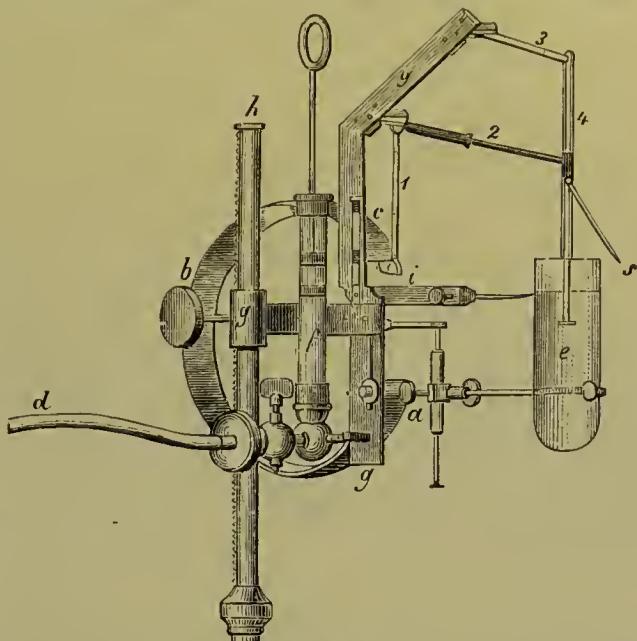


Fig. 116.

Fick's Spring Manometer, as improved by Hering.

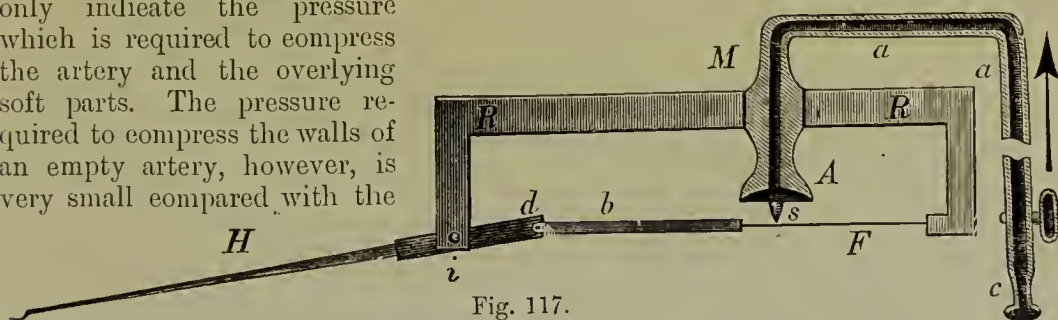


Fig. 117.

Fick's Flat Spring Kymograph.

blood-pressure. It is only 4 mm. Hg. V. Basch estimated the pressure in the radial artery of a healthy man to be 135 to 165 millimetres of mercury.

Variations.—In children the blood-pressure increases with age, height, and weight. In the superficial temporal artery, at 2 to 3 years, it is = 97 mm.; 12 to 13 years, 113 mm. Hg (*A. Eckert*, c. § 100). The blood-pressure is raised immediately after **bodily movements**; it is higher when a person is in the horizontal position than when sitting, and in sitting than in standing. After a cold as well as after a warm bath, the first effect is an increase of blood-pressure and of the quantity of urine.

85. BLOOD-PRESSURE IN THE ARTERIES.—The following results have been obtained by experiment on **systemic arteries** :—

(a) **Mean Blood-Pressure.**—The blood-pressure is very considerable, varying within pretty wide limits; in the large arteries of large mammals, and perhaps in man, it = 140 to 160 millimetres [5.4 to 6.4 inches] of a mercurial column.

The following results have been obtained, those marked thus * by Poiseuille, and those + by Volkmann :—

* Carotid, Horse 161 mm.	+ Carotid, Fowl, 88 to 171 mm.
+ „ „ 122 to 214 mm.	+ Aorta of Frog, 22 to 29 mm.
* „ „ Dog, 151 mm.	+ Gill Artery of Pike, 35 to 84 mm.
„ „ 130 to 190 mm. (<i>Ludwig</i>).	Braehial artery of Man during an operation, 110 to 120 mm. (<i>Faivre</i>). Perhaps too low owing to the injury.
+ „ „ Goat, 118 to 135 mm.	
+ „ „ Rabbit, 90 mm.	

E. Albert estimated the blood-pressure by means of a manometer, placed in connection with the anterior tibial artery of a boy whose leg was to be amputated, to be 100 to 160 mm. Hg. The elevation with each pulse-beat was 17 to 20 mm.; coughing raised it to 20 or 30 mm.; tight bandaging of the healthy leg, 15 mm.; while passive elevation of the body, whereby the hydrostatic action of the column of blood was brought into play, raised it 40 mm.

The pressure in the aorta of mammals varies from 200 to 250 mm. Hg. As a general rule, the blood-pressure in large animals is higher than in small animals, because in the former the blood-channel is considerably longer, and there is a greater resistance to be overcome. In very young and in very old animals the pressure is lower than in individuals in the prime of life.

The arterial pressure in the *fœtus* is scarcely half that of the newly born, while the venous pressure is higher, the difference of pressure between arterial and venous blood being scarcely half so great as in adult animals (*Cohnstein and Zuntz*).

The **arterial blood-pressure** is **highest** in the aorta, and falls towards the smaller vessels, but the fall is very gradual, as shown in fig. 118. A great fall takes place on passing from the area of the arterioles into the capillary area (C), while it is less in the venous area, and negative in the veins near the heart, as indicated in the dotted line passing below the abscissa, so that the pressure is **lowest** in the cardiac ends of the *venæ cavae* (compare fig. 124).

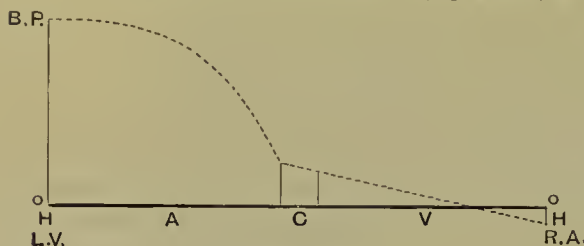


Fig. 118.

Scheme of the blood-pressure, in A, the arteries; C, capillaries, and V, veins; O-O is the abscissa or line of no pressure; L.V., left ventricle, and R.A., right auricle; B.P., the height of the blood-pressure.

(b) **Branching of the Blood-Vessels.**—Within the large arteries the blood-pressure diminishes relatively little as we pass toward the periphery, because the difference of

the resistance in the different sections of large tubes is very small. As soon, however, as the arteries begin to divide frequently, and undergo a considerable diminution in their lumen, the blood-pressure in them rapidly diminishes because the propelling energy of the blood is much weakened, owing to the resistance which it has to overcome (§ 99).

(c) **Amount of Blood.**—The blood-pressure is increased with *greater filling of the arteries*, and *vice versa*; hence it

Increases.

1. With increased and accelerated action of the heart;
2. In plethoric persons;
3. After a very considerable increase of the quantity of blood by direct transfusion, or after a copious meal.

Decreases.

1. During diminished and enfeebled action of the heart;
2. In anæmic persons;
3. After hæmorrhage or considerable excretions from the blood by sweating, the urine, severe diarrhœa.

The blood-pressure does not vary in the same proportion as the variations in the amount of blood. The vascular system, in virtue of its muscular tissue, has the property, within liberally wide limits, of accommodating itself to larger or smaller quantities of blood (*C. Ludwig and Worm Müller*, § 102, d). [In fact, a large amount of blood may be transfused without materially raising the blood-pressure. Small and moderate hæmorrhages (in the dog to 2·8 per cent. of the body-weight) have no obvious effect on the blood-pressure. After a slight loss of blood the pressure may even rise (*Worm Müller*). If a large amount of blood be withdrawn, it causes a great fall of the blood-pressure, and when hæmorrhage occurs to 4–6 per cent. of the body-weight, the blood-pressure = 0. The transfusion of a moderate amount of blood does not raise

the mean arterial blood-pressure. There are important practical deductions from these experiments, viz., that the arterial blood-pressure cannot be diminished directly by moderate blood-letting, and that the blood-pressure is not necessarily high in plethoric persons.]

(d) **Capacity of the Vessels.**—The arterial pressure rises when the capacity of the arterial system is diminished, and conversely. The circularly-disposed smooth muscular fibres of the arteries are the chief agents concerned in this process. When they relax, the arterial blood-pressure falls, and when they contract, it rises. These actions of muscular fibres are controlled and regulated by the action of the vasomotor nerves (§ 371).

(e) **Collateral Vessels.**—The arterial pressure within a *given area* of the vascular system must rise or fall according as the neighbouring areas are diminished, whether by the application of pressure, or a ligature, or are rendered impervious, or as these areas dilate. The application of cold or warmth to limited areas of the body—increasing or diminishing the atmospheric pressure on a part—the paralysis or stimulation of certain vasomotor areas all produce remarkable variations in the blood-pressure (§ 371). [The effect of dilatation of a large vascular area on the arterial pressure is well shown by what happens when the blood-vessels of the abdomen are dilated. Divide both vagi in the neck of a rabbit and stimulate the **central end** of the **superior cardiac** branch of the vagus or **depressor nerve**; after a few seconds the blood-vessels of the abdomen dilate, and gradually there is a steady fall of the blood-pressure in the systemic arteries. Fig. 119 is a blood-pressure tracing

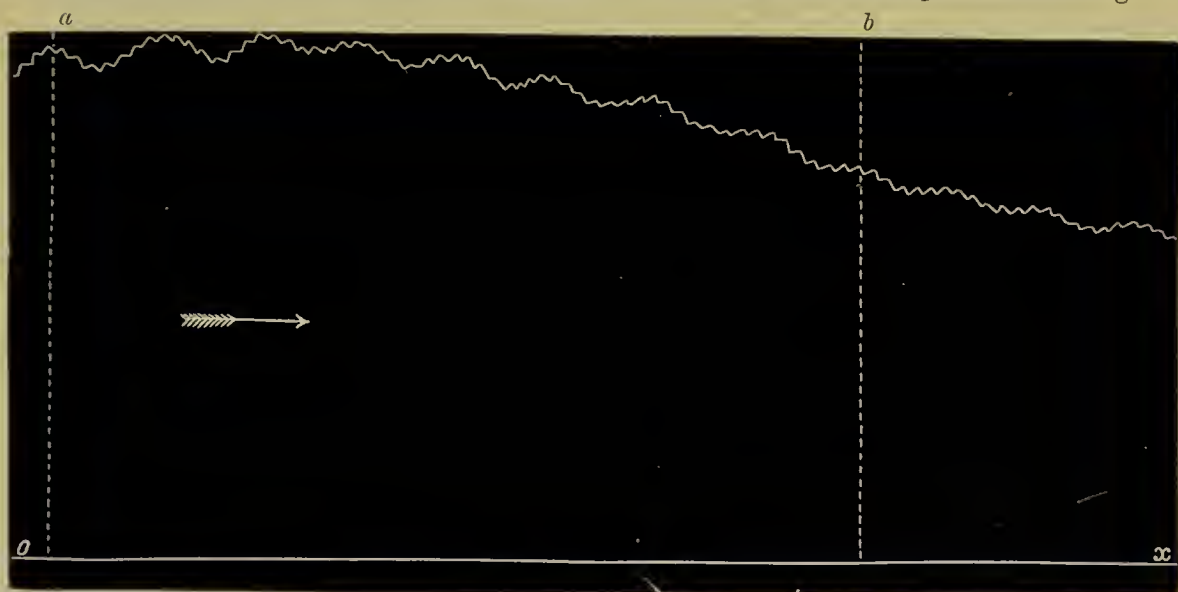


Fig. 119.

Kymographic tracing showing the effect on the blood-pressure of stimulation of the central end of the depressor nerve in the rabbit after section of both vagi in the neck. Stimulation began at *a* and ended at *b*; *o-x*, the abscissa.

showing the height of the blood-pressure before stimulation, *a*. The stimulation was continued from *a* to *b*, and after a rather long *latent* period there is a steady fall of the blood-pressure.

(f) **Respiratory Undulations.**—The arterial pressure also undergoes regular variations or undulations owing to the respiratory movements. These undulations are called *respiratory undulations* (figs. 115, 119, 120). Stated broadly, on the whole, during inspiration the blood-pressure rises, and during expiration it falls (§ 74). This is not strictly correct. These undulations may be explained by the fact that, with every expiration, the blood in the aorta is subjected to an increase of pressure through the compressed air in the chest; with every inspiration, on the

other hand, it is diminished owing to the rarefaction of the air in the lungs acting upon the aorta. Besides, the inspiratory movements of the chest aspirate blood from the venæ cavæ towards the heart, while expiration retards it, and thus influences the blood-pressure. The undulations are most marked in the arteries lying nearest to the heart. The respiratory undulations are due in part to a stimulation or condition of excitement of the vaso-motor centre, which runs parallel with the respiratory movements. This stimulation of the vaso-motor centre causes the arteries to contract, and thus the blood-pressure is raised. The variations in the pressure which depend upon a varying activity of the vaso-motor centre are known as the "curves of Traube and Hering." Fig. 120 shows the carotid blood-

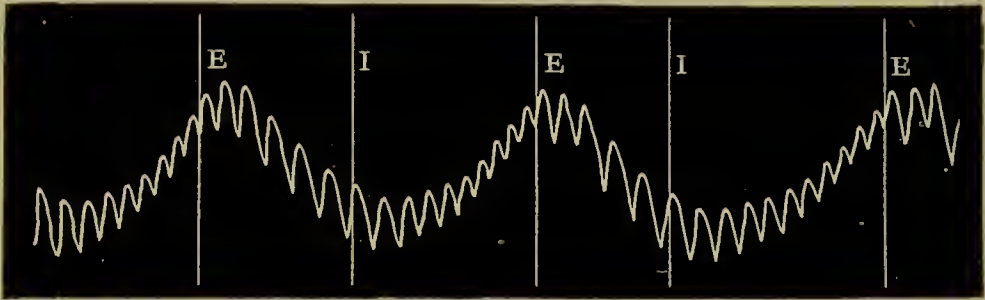


Fig. 120.

Carotid blood-pressure tracing of dog ; vagi not divided ; I = inspiration. E = expiration (*Stirling*).

pressure tracing of a dog. In this curve, when inspiration begins (I) the blood-pressure is still falling slightly, but gradually rises until it reaches its maximum shortly after the beginning of expiration (E). [The maxima and minima of the respiratory and blood-pressure curves do not coincide exactly, but in addition the *number* of pulse-beats is greater in the ascent than in the descent. This is well marked in a blood-pressure tracing from a dog's carotid (fig. 120) while in a rabbit this difference of the pulse-rate is but slightly marked (fig. 119). The smaller number of pulse-beats during the descent, *i.e.*, during the greater part of expiration, is due to the activity of the cardio-inhibitory centre in the medulla oblongata. This is proved by the fact that section of both vagi in the dog causes the difference of pulse-rate to disappear, while other conditions remain the same as before, except that the heart beats more rapidly. It would seem that, during the ascent, the cardio-inhibitory centre is comparatively inactive. It is clear, therefore, that the **respiratory** and **cardio-inhibitory centres** in the medulla oblongata act to a certain extent in unison, so that it is reasonable to suppose that other centres situated in close proximity to these may also act in unison with them, or, as it were, "in sympathy." As already stated, the **vaso-motor centre** is also in action during a particular part of the time.]

[If a dog be curarised and **artificial respiration** established, the respiratory undulations still occur, although in a modified form. In artificial respiration, the mechanical conditions, as regards the intra-thoracic pressure, are exactly the reverse of those which obtain during ordinary respiration. Air is forced into the chest during artificial respiration, so that the pressure within the chest is increased during inspiration, while in ordinary inspiration the pressure is diminished. Thus, the same mechanical explanation will not suffice for both cases.]

If the artificial respiration be suddenly interrupted in a curarised animal, the blood-pressure rises steadily and rapidly. This rise is due to the stimulation of the vaso-motor centre in the medulla oblongata by the impure blood. This causes contraction of the small arteries throughout the body, which retards the outflow

from the large arteries, and thus the pressure within them is raised. [Stated broadly, the arterial pressure depends on the **central organ**—the **heart**, and on the condition of the **peripheral organs**—the **small arteries**. Both are influenced by the nervous system. If the action of the vaso-motor centre be eliminated by dividing the spinal cord in the cervical region, arrest of the respiration causes a very slight rise of the blood-pressure; hence, it is evident that venous blood acts but slightly on the heart, or on any local peripheral nervous mechanism, or on the muscular fibres of the arteries. This experiment shows that it is the vaso-motor centre which is specially acted upon by the venous blood.]

[Traube-Hering Curves.—The following experiment proves that the varying activity of the vaso-motor centre suffices to produce undulations in the blood-pressure tracing. In a curarised dog expose both vagi; establish artificial respiration; and estimate the blood-pressure in the carotid. After section of the vagi, the heart will beat more rapidly, but it will be undisturbed by the cardio-inhibitory centre. Thus the *central* factor in the causation of the blood-pressure remains constant. Suddenly interrupt the respiration, and, as already stated, the blood-pressure will rise steadily and uniformly, owing to the stimulation of the vaso-motor centre by the venous blood. In this case the *peripheral* factor, or state of tension of the small arteries throughout the body, is influenced by the condition of the nerve-centre, which controls their action. After a time, the blood-pressure tracing shows a series of bold curves higher than the original tracing. These can only be due to an alteration in the state of the small arteries, brought about by a condition of rhythmical activity of the vaso-motor centre. These curves were described and figured by Traube, and are called the Traube or Traube-Hering curves. As in other conditions, stimulation causes exhaustion, and soon the venous blood paralyses the vaso-motor centre, and the small arteries relax, blood flows freely out of the larger arteries, and the blood-pressure rapidly sinks. Variations in the blood-pressure have been observed after a mechanical pump has been substituted for the heart, *i.e.*, after all respiratory movements have been set aside, so that the only factor which would account for the phenomena of the Traube-Hering curves is the variation in the peripheral resistance in the small arteries, determined by the condition in the vaso-motor centre.]

Variations.—The respiratory undulations of the blood-pressure become more pronounced the greater the force of the respirations, which produce greater variations of the intra-thoracic pressure. In man, the diminution of the pressure within the trachea is 1 mm. Hg. during tranquil inspiration, while during forced respiration, when the respiratory passage is closed, it may be 57 mm. Conversely, during ordinary expiration, the pressure is increased within the trachea 2-3 mm. Hg, while during forced expiration, owing to the compression of the abdominal muscles, it may reach 87 mm. Hg.

Other Factors.—The increase of the blood-pressure during inspiration, as well as the fall during expiration, must in part depend upon the pressure within the abdomen. As the diaphragm descends during inspiration, it presses upon the abdominal contents, including the abdominal vessels, whereby the blood-pressure must be increased. The reverse effect occurs during expiration (*Schweinburg*). [Section of both phrenic nerves and opening of the abdominal cavity cause the respiratory undulations almost entirely to disappear. The respiratory undulations, therefore, depend in great part upon the changes of the abdominal pressure and the effect of these changes on the amount of blood in the abdominal vessels. When making a blood-pressure experiment, pressure upon the abdomen of the animal with the hand causes the blood-pressure to rise rapidly.]

Kronecker and Heinrichs ascribe the undulations to mechanical causes, and as due to the simultaneous compression of the heart by the lungs during respiration. Everything which hinders the diastole of the heart diminishes the blood-pressure. As soon, therefore, as the lungs during inspiration have become distended so far as to compress the heart, the diastole is affected, and thereby a decrease in the blood-pressure of the aorta is brought about. As soon as air passes out of the lungs, and the latter retract, the heart becomes fuller and the arterial pressure rises.

(g) **Variations with each Pulse-Beat.**—The mean arterial pressure undergoes a variation with each heart-beat or *pulse-beat*, causing the so-called **pulsatory**

undulations (fig. 120). The mass of blood forced into the arteries with each ventricular systole causes a positive wave and an increase of the pressure corresponding with it, which of course corresponds in its development and in its form with the pulse-curve.

In the large arteries Volkmann found the increase during the heart-beat to be $\approx \frac{1}{17}$ (horse) and $\frac{1}{17}$ (dog) of the total pressure.

None of the apparatus described in § 84 gives an exact representation of the pulse-curve. They all show simply a rise and fall, a simple curve. The sphygmograph alone gives a true expression of the undulations in the blood-pressure which are due to the heart-beat.

§(h) **Arrest of the Heart's Action.**—If the heart's action be arrested or interrupted by continued **stimulation of the vagus**, or by high positive respiratory pressure, the arterial blood-pressure falls enormously, while it rises in the veins as the blood flows into them from the arteries to equilibrate the difference of pressure in the two sets of vessels. This experiment shows that, even when the difference of pressure is almost entirely set aside, the passive blood presses upon the arterial walls, *i.e.*, on account of the overfilling of the blood-vessels a slight pressure is exerted upon the walls, even when there is no circulation. [As already stated, the arterial pressure depends on the condition of the central organ—the heart—and on the peripheral organs—the small arteries. If the action of the heart be arrested, then the blood-pressure rapidly falls. Fig. 121 shows the effect on the blood-pressure

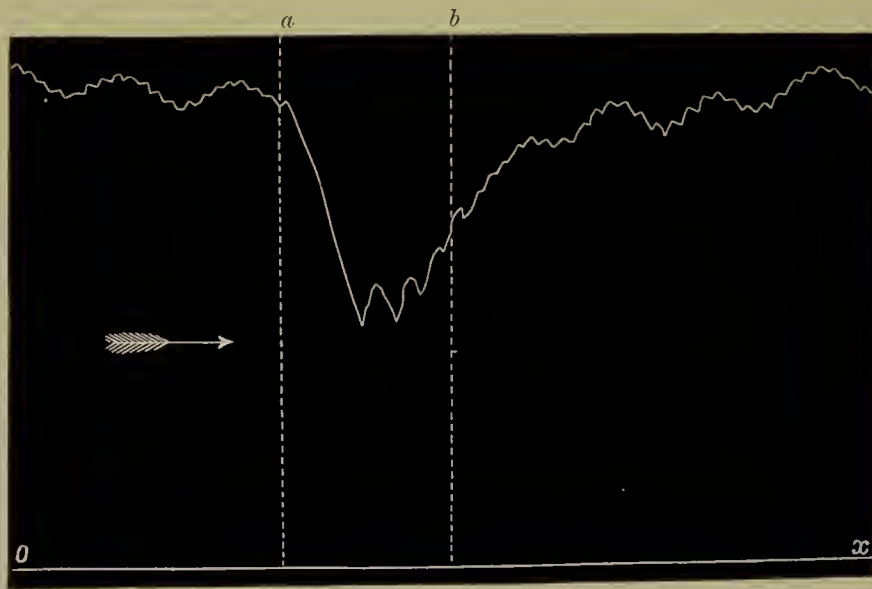


Fig. 121.

Blood-pressure tracing taken with a mercurial kymograph from the carotid of a rabbit.
0-x, abscissa ; stimulation of vagus begun at *a* and stopped at *b*.

of arresting the action of the heart by stimulation of the **peripheral end of the vagus** in a rabbit. There is a sudden fall of the arterial pressure, as shown by the rapid fall of the curve from *a*.]

[**Variations in Animals.**—The pressure in the arterial system depends upon the balance between the inflow and outflow, *i.e.*, upon the heart and the state of the arterioles. But it is to be noted that the central factor, the heart, varies in different animals. In the rabbit the heart normally beats rapidly, so that section of the vagi does not cause any great increase in the number of beats, nor is the blood-pressure much raised thereby. In the dog, on the other hand, the beats are considerably increased by section of the vagi, while the blood-pressure rises considerably. Atropin paralyses the cardiac terminations of the vagus, and thereby trebles the number of heart-beats in the dog, while it only raises it 25 per cent. in the rabbit ; in man, again, the number may be doubled. As Brunton has shown, this difference of the initial number of heart-beats and the action of the vagus have important relations to the action of

drugs on the blood-pressure. For example, if an intact rabbit be caused to inhale amyl nitrite the blood-pressure falls at once and rapidly, while in the dog the fall may be slight. The pulse of the dog, however, is greatly accelerated, so much so as to be nearly as rapid as that of the rabbit. In both, the vessels are dilated, but in the dog, notwithstanding this dilatation, which *per se* would cause the pressure to fall, the heart of the dog beats now so rapidly as to compensate for this, and thus keeps the blood-pressure nearly normal; while the increased rate of beating in the rabbit is not sufficient for this purpose. If the vagi in the dog be divided, the subsequent inhalation of amyl nitrite causes a fall of blood-pressure like that in the rabbit (*Brunton*). Fig. 122 shows that the arterial tension has no direct relation to the position of an animal in the zoological scale.]

[**Relation of Blood-Pressure to Pulse-Rate.**—When the blood-pressure rises in an intact animal, as a rule the pulse-rate falls, owing to stimulation of the vagus centre increasing the cardio-inhibitory action, while a fall of blood-pressure is accompanied by an increase of the number of pulse-beats for the opposite reason, the action of the medullary cardio-inhibitory centre being increased. But the blood-pressure may be increased either by the action of the heart or the arterioles. If we divide the vagi the pulse beats more quickly, and in some animals the blood-pressure rises; in this case, the rise in the two curves occurs together, and if the vagi be stimulated there is a sudden fall of the blood-pressure, due to arrest of the heart's action, so that again the two curves are parallel. If the arterioles contract the blood-pressure rises, but by and by the pulse-rate falls, owing to the cardio-inhibitory action of the vagus; while on the other hand, if the arterioles are dilated, the blood-pressure falls, and the heart beats faster. Thus, in both of these cases the pulse-curve and blood-pressure curve run in opposite directions. These results only obtain when the vagi are intact (*Brunton*).]

[The increase in the pulse-rate and blood-pressure following section of the vagi do not run parallel. Both sooner or later reach a maximum, but the blood-pressure gradually falls to or below the normal while the pulse-rate remains above the normal (*Münzel*).]

For the effects of the nervous system upon the blood-pressure, see § 371.

Pathological.—In persons suffering from granular or contracted kidney and sclerosis of the arteries, in lead-poisoning, and after the injection of ergotin, which causes contraction of the small arteries, it is found, on employing the method of v. Basch, that the blood-pressure is raised. It is also increased in cases of cardiac hypertrophy with dilatation, and by digitalis in cardiac affections, while it falls after the injection of morphia. The blood-pressure falls in fever, a fact also indicated in the sphygmogram (§ 69), and it is low in chlorosis and phthisis.

86. BLOOD-PRESSURE IN THE CAPILLARIES.—**Methods.**—Direct estimation of the capillary pressure is not possible on account of the smallness of the capillaries. If a glass plate of known dimensions be placed on a vascular portion of the skin, and if it be weighted until the capillaries become pale, we obtain approximately the pressure necessary to overcome the capillary pressure. N. v. Kries placed a small glass plate (fig. 123) 2.5–5 sq. mm., on the skin at the root of the nail on the terminal phalanx, or on the ear in man, and on the gum in rabbits. Into a scale-pan attached to this weights were placed until the skin became pale. The pressure in the capillaries of the hand, when the hand is raised, Kries found to be 24 mm. Hg.; when the hand hangs down, 54 mm. Hg.; in the ear, 20 mm.; and in the gum of a rabbit, 32 mm.



Fig. 122.

Blood-pressure tracings from different animals. The scale of centimetres is reduced one-half.

Roy and Graham Brown compressed from below transparent vascular membranes against a glass plate by means of an elastic bag connected with a manometer, while the variations in the capillaries were observed from above by a microscope.

Conditions influencing Capillary Pressure.—The capillary blood-pressure in a given area **increases**—(1) When the afferent small arteries dilate, so that the blood-pressure within the large arteries is propagated more easily into them. (2) By increasing the pressure in the small afferent arteries. (3) By narrowing the diameter of the veins leading from the capillary area. Closure of the veins may quadruple the pressure. (4) By increasing the pressure in the veins, *e.g.*, by altering the position of a limb. A **diminution** of the capillary pressure is caused by the opposite conditions.



Fig 123.

V. Kries's apparatus for capillary pressure. *a*, square of glass.

Changes in the **diameter of the capillaries** influence the internal pressure. We have to consider the movements of the capillary wall itself as well as the pressure, swelling, and consistence of the surrounding tissues. The resistance to the blood-stream is greatest in the capillary area, and it is evident that the blood in a long capillary must exert more pressure at the commencement than at the end of the capillary; in the middle of the capillary area the blood-pressure is just about one-half of the pressure within the large arteries (*Donders*). The capillary pressure must also vary in different regions of the body. Thus, the pressure within the intestinal capillaries, in those constituting the glomeruli of the kidney, and in those of the lower limbs when a person is in the erect posture, must be greater than in other regions, depending in the former cases partly upon the double resistance caused by two sets of capillaries, and in the latter case partly on purely hydrostatic causes.

87. Blood-Pressure in the Veins.—In the **large venous trunks** near the heart (innominate, subclavian, jugular) a mean **negative pressure** of about -0.1 mm. Hg. prevails (*H. Jacobson*). Hence, the lymph-stream can flow unhindered. As the distance of the veins from the heart increases, there is a *gradual* increase of the lateral pressure; in the external facial vein (sheep) $= +3$ mm.; brachial, 4.1 mm., and in its branches 9 mm.; crural, 11.4 mm. [The pressure is said to be *negative* when it is less than that of the atmosphere. The gradual fall of the blood-pressure from the capillary area (C) to the venous area (V) is shown in fig. 124, while within the thorax, where the veins terminate in the right auricle, the pressure is negative.]

Modifying Conditions.—(1) All conditions which *diminish the difference of pressure* between the arterial and venous systems *increase the venous pressure*, and *vice versa*.

(2) General plethora of blood increases it; anæmia diminishes it.

(3) Respiration, or the **aspiration of the thorax**, affects specially the pressure in the veins near the heart; during inspiration, owing to the diminished tension, blood flows towards the chest, while during expiration it is retarded. The effects are greater the deeper the respiratory movement, and these may be very great when the respiratory passages are closed (§ 60).

[When a vein is exposed at the root of the neck, it collapses during inspiration, and fills during expiration. The respiratory movements do not affect the venous stream in peripheral veins. The veins of the neck and face become distended with blood during crying, and on making violent expiratory efforts, as in blowing upon a wind instrument. Every surgeon is acquainted with the fact that air is particularly liable to be sucked into the veins during inspiration in operations near the root of the neck. This is due to the negative intra-thoracic pressure occurring during inspiration.]

(4) **Aspiration of the Heart.**—Blood is sucked or aspirated into the auricles when they dilate (p. 66), so that there is a double aspiration—one synchronous with inspiration, and the other, which is but slight, synchronous with the heart-beat. There is a corresponding retardation of the blood-stream in the venæ cavæ, caused by the contraction of the auricle (p. 67, *a*). The respiratory and cardiac

undulations are occasionally observable in the jugular vein of a healthy person (§ 99).

(5) Change in the *position* of the limbs or of the body, for hydrostatic reasons, greatly alters the venous pressure. The veins of the lower extremity bear the greatest pressure, and Bardeleben has shown that the walls of these veins contain much smooth muscle (§ 65). Hence, when these muscles from any cause become insufficient, dilatations occur in the veins, giving rise to the production of **varicose veins**.

[Braune showed that the femoral vein under Ponpart's ligament collapsed when the lower limb was rotated outwards and backwards, but filled again when the limb was restored to its former position. All the veins which open into the femoral vein have valves, which permit blood to pass into the femoral vein, but prevent its reflux. This mechanism acts to a slight degree as a kind of suction and pressure apparatus when a person walks, and thus favours the onward movement of the blood.]

[(6) **Muscular Movements.**—Veins which lie between muscles are compressed when these muscles contract, and as valves exist in the veins, the flow of blood is accelerated towards the heart; if the outflow of the blood be obstructed in any way, then the venous pressure on the distal side of the obstruction may be greatly increased. When a fillet is tied on the upper-arm, and the person moves the muscles of the fore-arm, the superficial veins become turgid, and can be distinctly traced on the surface of the limb.]

(7) **Gravity** exercises a greater effect upon the blood-stream in the extensile veins than upon the stream in the arteries. It acts on the distribution of the blood, and thus indirectly on the motion of the blood-stream. It favours the emptying of descending veins, and retards the emptying of ascending veins, so that the pressure becomes less in the former and greater in the latter. If the position of the limb be changed, the conditions of pressure are also altered. If a person be suspended with the head hanging downwards, the face soon becomes turgid, the position of the body favouring the inflow of blood through the arteries and retarding the outflow through the veins. If the hand hangs down it contains more blood in the veins than if it is held for a short time over the head, when it becomes pale and bloodless. [As Lister has shown, the condition of the vessels in the limb is influenced not only by the position of the limb, but also by the fact that a nervous mechanism is called into play.]

[**Ligature of the portal vein** causes congestion of the rootlets and dilatation of all the blood-vessels in the abdomen; gradually nearly all the blood of the animal accumulates within its belly, so that, paradoxical as it may seem, an animal may be bled into its own belly. As a consequence of *sudden* and *complete* ligature of this vein, the arterial blood-pressure gradually and rapidly falls, and the animal dies very quickly. If the ligature be removed before the blood-pressure falls too much, the animal may recover. Schiff and Lantenbach regard the symptoms as due chiefly to the action of a poison, for when the blood of the portal vein in an animal treated in this way is injected into a frog, it causes death within a few hours, while the ordinary blood of the portal vein has no effect.]

[**Ligature of the Veins of a Limb.**—The effect of ligaturing or compressing *all* the veins of a limb is well seen in cases where a bandage has been applied too tightly. It leads to congestion and increase of pressure within the veins and capillaries, increased transudation of fluid through the capillaries, and consequent *œdema* of the parts beyond the obstruction. Ligature of *one* vein does not always produce *œdema*, but if several veins of a limb be ligatured, and the vaso-motor nerves be divided at the same time, the rapid production of *œdema* is ensured. In

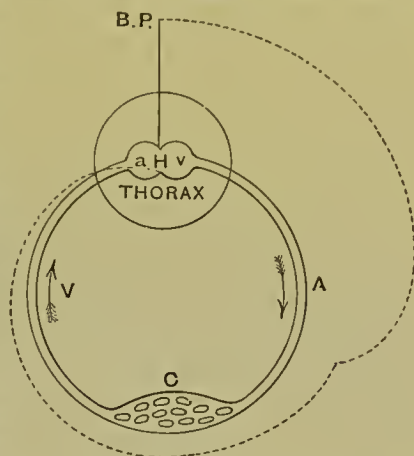


Fig. 124.

Scheme of the blood-pressure. H, heart; a, auricle; v, ventricle; A, arterial; C, capillary; and V, venous areas. The circle indicates the parts within the thorax; B.P., pressure in the aorta.

pathological cases the pressure of a tumour upon a large vein may produce similar results (§ 203).]

88. BLOOD-PRESSURE IN THE PULMONARY ARTERY.—Methods.—(1) Direct estimation of the blood-pressure in the pulmonary artery by opening the chest was made by C. Ludwig and Bentner (1850). Artificial respiration was kept up, and the manometer was placed in connection with the left branch of the pulmonary artery. The circulation through the left lung of cats and rabbits was thereby completely cut off, and in dogs to a great extent interrupted. There was an additional disturbing element, viz., the removal of the elastic force of the lungs, owing to the opening of the chest, whereby the venous blood no longer flowed normally into the right heart, while the heart itself was under the full pressure of the atmosphere. The estimated pressure in the dog=29·6; in the cat=17·7; in the rabbit=12 mm. Hg., *i.e.*, in the dog 3 times, the rabbit 4 times, and the cat 5 times less than the carotid pressure.

(2) Hering (1850) experimented upon a calf with ectopia cordis. He introduced glass tubes directly into the heart, by pushing them through the muscular walls of the ventricles. The blood rose to the height of 21 inches in the right tube, and 33·4 inches in the left.

(3) Faivre (1856) introduced a catheter through the jugular vein into the right ventricle, and placed it in connection with a recording tambour.

Indirect measurements have been made by comparing the relative thickness of the walls of the right and left ventricles, or the walls of the pulmonary artery and aorta.

Beutner and Marey estimated the relation of the pulmonary artery to the aortic pressure as 1 to 3; Goltz and Gaule as 2 to 5; Fick and Badoud found a pressure of 60 mm. in the pulmonary artery of the dog, and in the carotid 111 mm. Hg. The blood-pressure within the pulmonary artery of a child is relatively higher than in the adult.

Elastic Tension of Lungs.—The lungs within the chest are kept in a state of distention, owing to the fact that a negative pressure exists on their outer pleural surface. When the glottis is open, the inner surface of the lung and the walls of the capillaries in the pulmonary air-vesicles are exposed to the full pressure of the air. The heart and large blood-vessels within the chest are not exposed to the full pressure of the atmosphere, but only to the pressure which corresponds to the atmospheric pressure *minus* the pressure exerted by the elastic traction of the lungs (§ 60). The trunks of the pulmonary artery and veins are subjected to the same conditions of pressure. The elastic traction of the lungs is greater the more they are distended. The blood of the pulmonary capillaries will, therefore, tend to flow towards the large blood-vessels. As the elastic traction of the lungs acts chiefly on the thin-walled pulmonary veins, while the semi-lunar valves of the pulmonary artery, as well as the systole of the right ventricle, prevent the blood from flowing backwards, it follows that *the blood in the capillaries of the lesser circulation must flow towards the pulmonary veins.*

If tubes with thin walls be placed in the walls of an elastic distensible bag, the lumen of these tubes changes according to the manner in which the bag enclosing them is distended. If the bag be directly inflated so as to increase the pressure within it, the lumen of the tubes is diminished (*Funke and Latschenberger*). If the bag be placed within a closed space, and the tension within this space be diminished so that the bag thereby becomes distended, the tubes in its wall dilate. In the latter case—viz., by negative aspiration—the lungs are kept distended within the thorax, hence the blood-vessels of the lungs containing air are wider than those of collapsed lungs (*Quincke and Pfeiffer, Bowditch and Garland, De Jüger*). Hence also more blood flows through the lungs distended within the thorax than through collapsed lungs. The *dilatation* which takes place during *inspiration* acts in a similar manner. The negative pressure that obtains within the lungs during inspiration causes a considerable dilatation of the pulmonary veins, into which the blood of the lungs flows readily, whilst the blood under high pressure in the thick-walled pulmonary artery scarcely undergoes any alteration. The velocity of the blood-stream in the pulmonary vessels is accelerated during inspiration (*De Jüger, Lalesque*). The blood-pressure in the pulmonary circuit is raised when the lungs are inflated. Contraction of small arteries, which causes an

increase of the blood-pressure in the systemic circulation, also raises the pressure in the pulmonary circuit, because more blood flows to the right side of the heart.

The vessels of the pulmonary circulation are very distensible and their **tonus** is slight. [Occlusion of one branch of the pulmonary artery does not raise the pressure within the aorta. Even when one pulmonary artery is plugged with an embolon of paraffin, the pressure within the aortic system is not raised (*Lichtheim*). When a large branch of the pulmonary artery becomes impervious, the obstruction is rapidly compensated for, and this is not due to the action of the nervous system. The vaso-motor system has much less effect upon the pulmonary blood-vessels than upon those of the systemic circulation. The compensation seems to be due chiefly to the great distensibility and dilatation of the pulmonary vessels (*Lichtheim*).] We know little of the effect of physiological conditions upon the pulmonary artery. According to *Lichtheim suspension of the respiration* causes an increase of the pressure. [In one experiment he found that the pressure within the pulmonary artery was increased, while it was not increased in the carotid, and he regards this experiment as proving the existence of vaso-motor nerves in the lung. While asphyxia increases enormously the blood-pressure in the systemic arteries, it has very little or no effect on the pressure as measured in the pulmonary system, although the latter is provided with vaso-motor nerves (§ 371).]

During the act of great straining the blood at first flows rapidly out of the pulmonary veins, and afterwards ceases to flow, because the inflow of blood into the pulmonary vessels is interfered with. As soon as the straining ceases, blood flows rapidly into the pulmonary vessels (*Lalesque*).

Severini found that the blood-stream through the lungs is greater and more rapid when the lungs are filled with air rich in CO_2 than when the air within them is rich in O. He supposes that these gases act upon the vascular ganglia within the lung, and thus affect the diameter of the vessels.

Pathological.—Increase of the pressure within the area of the pulmonary artery occurs frequently in man, in certain cases of heart disease. In these cases the second pulmonary sound is always accentuated, while the elevation caused thereby in the cardiogram is always more marked and occurs earlier (§ 52). Electrical and mechanical stimulation of abdominal organs raises the blood-pressure in the pulmonary artery (*Morel*).

[The action of drugs on the pulmonary circulation may be tested by Holmgren's apparatus (§ 94), which permits of distention of the lung and retention of the normal circulation in the frog. Cold contracts the pulmonary capillaries to one-third of their diameter, and anæsthetics arrest the pulmonary circulation, chloroform being most and ether least active, while ethidene is intermediate in its effect.]

[Influence of the Nervous System on the Pulmonary Circulation.]—It is much less dependent on the nervous system than the systemic circulation, but recent experiments have shown that the pulmonary vessels are supplied by vaso-motor nerves through the roots of the uppermost (2–7) dorsal nerves (§ 371). Very considerable variations of the blood-pressure within the other parts of the body may occur, while the pressure within the right heart and pulmonary artery is but slightly affected thereby. The pressure is increased by electrical stimulation of the medulla oblongata, and it falls when the medulla is destroyed. Section and stimulation of the central or peripheral ends of the vagi, stimulation of the splanchnics, and of the central end of the sciatic, have but a minimal influence on the pressure of the pulmonary artery (*Aubert*).]

[Relation of pressure in pulmonary and systemic circulations.]—If the blood-pressure be measured simultaneously, in a eurarisid dog, in the carotid, and in a branch of the pulmonary artery—the chest being opened and artificial respiration being kept up—it is found that the pulmonary circulation is comparatively independent of the systemic, and alterations in the blood-pressure of the latter must be of large amount to affect the pulmonary blood-pressure. While stimulation of the peripheral end of the splanchnic nerve raised the pressure from 50 mm. Hg. in the carotid to 104 mm., it raised that in the pulmonary artery from 13 to 16 mm. Hg. Even stimulation of the lower end of the divided spinal cord, which

raised the carotid pressure from 52 to 232 mm. (*i.e.*, quadrupled it) only raised the pulmonary artery blood-pressure from 20 to 26 mm. The rise in the pulmonary blood-pressure is but a small fraction of the total pulmonary artery pressure. The increased pressure in the aortic system must be of considerable duration to effect the rise in the pulmonary vessels.]

[If the anterior roots of the dorsal nerves—between the second and seventh dorsal nerves—be stimulated, an increase is obtained in the pulmonary artery blood-pressure. This is due to the vaso-motor nerves, or **vaso-constrictor nerves** for the lungs, which leave the cord by these channels. The vaso-motor mechanism of the mammalian lung is but poorly developed as compared with that regulating the systemic arteries. Asphyxia, of course, raises the systemic pressure enormously, but it also raises that in the pulmonary artery, and the rise lasts longer in the latter than in the former. No vaso-motor nerves are conveyed by the vagi to the lungs (*Bradford and Dean*).]

89. VELOCITY OF THE BLOOD-STREAM.—

Methods: (1) A. W. Volkmann's Hæmadrometer (1850).—A glass tube of the shape of a hair-pin, 60–130 cm. long and 2 or 3 mm. broad, with a scale attached to it, is fixed to a metallic basal plate, B, so that each limb passes to a three-wayed stop-cock. The basal plate is perforated along its length, and carries at each end short cannulæ, *c, c*, which are tied into the ends of a divided artery. The whole apparatus is first filled with salt solution. The stop-cocks are moved simultaneously, as they are attached to a toothed wheel, and have at first the position given in fig. 125, I, so that the blood simply flows through the passage in the basal piece, *i.e.*, directly from one end of the artery to the other. If at a given moment the stop-cock is turned in the direction indicated in fig. 125, II, the blood has to pass through the glass tube, and the time it takes to make the circuit is noted; and as the length of the tube is known, we can easily calculate the velocity of the blood. The method has very obvious defects arising from the narrowness of the tube; the introduction of such a tube offers new resistance, while there are no respiratory or pulse-variations observable in the stream in the glass tube.

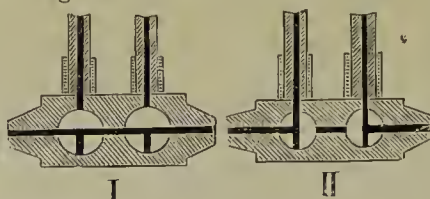
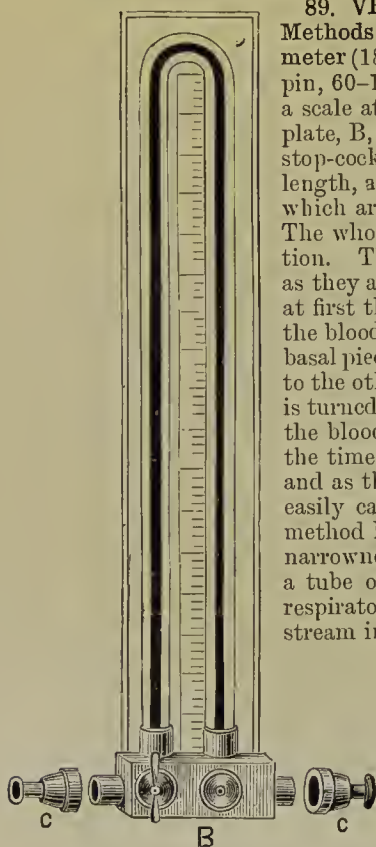


Fig. 125.

Volkmann's hæmadrometer (B). I, blood flows from artery to artery; II, blood must pass through the glass tube of B; *c, c*, cannulæ for the divided artery.

Volkmann found the **velocity** in the carotid (dog) = 205 to 357 mm. [10–12 inches]; carotid (horse) = 306; maxillary (horse) = 232; metatarsal = 56 mm. per second.

(2) C. Ludwig and Dogiel (1867) devised a "**stromuhr**" or **rheometer** for measuring the amount of blood which passed through an artery in a given time (fig. 126).

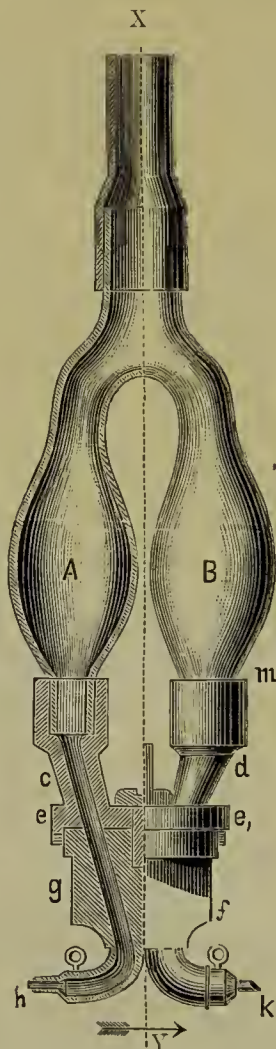


Fig. 126.

Ludwig and Dogiel's rheometer. X, Y, axis of rotation; A, B, glass bulbs; *h, k*, cannulæ inserted in the divided artery; *c, c*, rotates on *g, f*; *c, d*, tubes.

It consists of two glass bulbs, A and B, of exactly the same capacity. These bulbs communicate with each other above, their lower ends being fixed by means of the tubes, *c* and *d*, to the metal disc, *e*, *e*₁. This disc rotates round the axis, X, Y, so that, after a complete revolution, the tube *c* communicates with *f*, and *d* with *g*; *f* and *g* are provided with horizontally placed cannulae, *h* and *k*, which are tied into the ends of the divided artery. The cannula *h* is fixed in the central end, and *k* in the peripheral end of the artery (*e.g.*, carotid); the bulb, A, is filled with oil, and B with defibrinated blood; at a certain moment the communication through *h* is opened, the blood flows in, driving the oil before it, and passes into B, while the defibrinated blood flows through *k* into the peripheral part of the artery. As soon as the oil reaches *m*—a moment which is instantly noted, or, what is better, inscribed upon a revolving cylinder—the bulbs, A, B, are rotated upon the axis X, Y, so that B comes to occupy the position of A. The same experiment is repeated, and can be continued for a long time. The quantity of blood which passes in the unit of time (1 sec.) is calculated from the time necessary to fill the bulb with blood. Important results are obtained by means of this instrument.

[Suppose the capacity of the bulb to be 5000 cubic millimetres, and that it was filled in 10 secs., then 500 cubic millimetres are discharged in 1 sec. The velocity (V)=quantity or volume of blood, (*v*) divided by the sectional area of the vessel (*s*), *i.e.*, $V = \frac{v}{s}$ therefore the

velocity $V = \frac{500 \text{ cubic millimetres}}{3.14} = 159 \text{ mm. per second.}$ In this case the diameter of the tube is taken as 2 mm., so that the sectional area of the artery is equal to 3.14 mm. The sectional area is calculated from the diameter of the circular tube by the following formula: the sectional area $s = \frac{3.14}{4} d^2$ when *d* is the diameter of the tube; or $s = \pi r^2$, where $\pi = 3.1416$, *r*=radius. Or the sectional area (*s*) is equal to the $d^2 \times 0.7854$, *i.e.*, $4 \times 0.7854 = 3.1416$.

[As albumose injected into the blood prevents it from coagulating (dog), this fact has been turned to account in using the rheometer.]

(3) Vierordt's Hæmatometer (1858) consists of a small metal box (fig. 127, I) with parallel glass sides. To the narrow sides of the box are fitted an inlet *e*, and an exit cannula, *a*. In

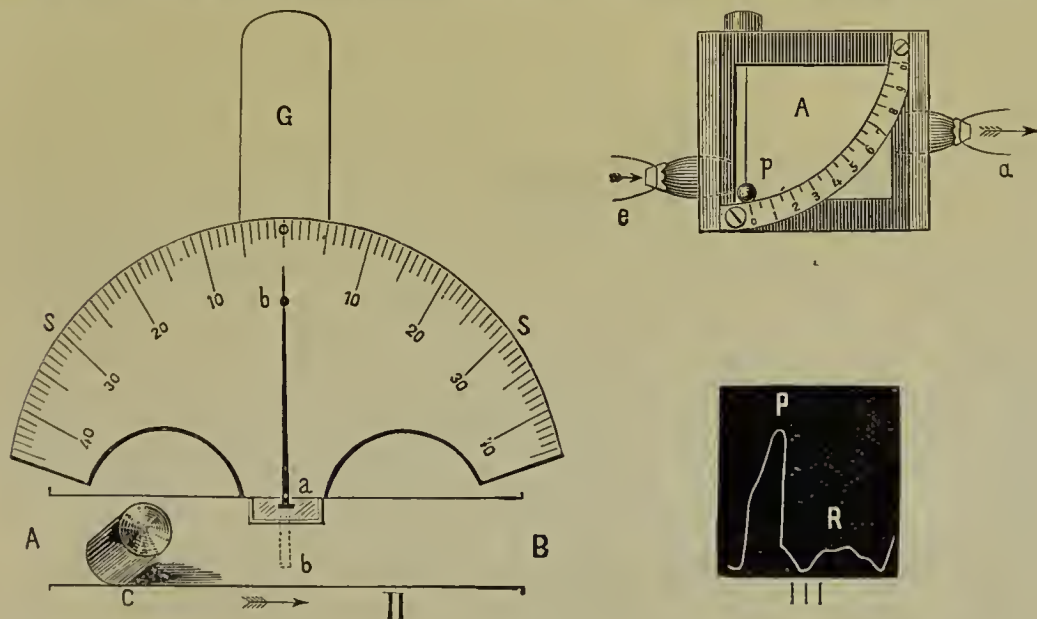


Fig. 127.

- I. Vierordt's hæmatometer. A, glass; *e*, entrance, *a*, exit cannula; *p*, pendulum.
 II. Dromograph. A, B, tube inserted in artery; C, lateral tube connected with a manometer; *b*, index moving in a caoutchouc membrane, *a*; G, handle. III. Curve obtained by dromograph.

its interior is suspended, against the entrance opening, a pendulum, *p*, whose vibrations may be read off on a curved scale. [This instrument, as well as Volkmann's apparatus, has only an historical interest.]

(4) Chauveau and Lortet's Dromograph (1860) is constructed on the same principle. A tube, A, B (fig. 127, II.), of sufficient diameter, with a side tube fixed to it, C, which can be placed in connection with a manometer, is introduced into the carotid artery of a horse. At *a* a small piece

is cut out and provided with a covering of gutta-percha which has a small hole in it; through this a light pendulum, α , b , with a long index, b , projects into the tube, *i.e.*, into the blood-current, which causes the pendulum to vibrate, and the extent of the vibrations can be read off on a scale, S , S . G is an arrangement to permit the instrument to be held. Both this and the former instrument are tested beforehand with a stream of water sent through them with varying velocities.

The curve of the velocity may be written off on a smoked glass plate, moving parallel with the index b . The dromograph curve, III, shows the primary elevation, P , and the dirotic elevation R .

(5) **Cybulski's Photohæmatometer.**—When fluid flows into a tube (fig. 128, II, *de*) in the direction of the arrow, the fluid stands higher in the manometer p than in m . The tube my indicates the lateral pressure, but px gives this *plus* the velocity of the fluid (p. 103). The velocity of the current may be estimated from the difference in the level in the two tubes.

Pitot's tube as used by *Cybulski* is bent at a right angle (I, *cp*), the end c being inserted and tied into the central, and p into the peripheral, part of a divided artery. As the blood flows through the tube, the blood rises higher in a than b .

To avoid having the manometers a and b too long, they are connected with each other by a capillary tube filled with air and provided above with a stop-cock i . The blood is allowed to rise to the height of 1 and 2, the stop-cock i is closed, and practically an air-manometer is made, which shows a marked difference in the level of the blood of the two tubes. The level of the blood in 1 and 2 is continually changed by the movements of the heart and those of respiration, and these variations are photographed by means of a camera n with a rapidly moving plate, K .

Fig. C shows a curve obtained from the carotid of a dog. The velocity of the current at $l_1-1=238$ mm., in the phase $2_1-2=225$ mm., and at $3_1-3=177$ mm. The velocity is greatest at the end of inspiration and the beginning of expiration. Asphyxia increases it at first. Paralysis of the sympathetic increases it, while stimulation of this nerve diminishes it. Section of the vagi increases the velocity, while their stimulation of course diminishes it.

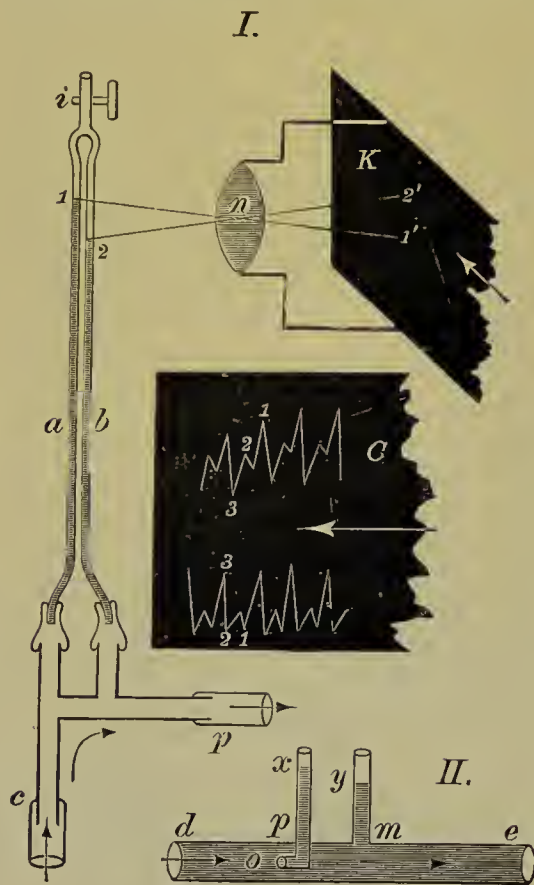


Fig. 128.

I. Scheme of the photohæmatometer; II. Pitot's tube.

Fig. C shows a curve obtained from the carotid of a dog. The velocity of the current at $l_1-1=238$ mm., in the phase $2_1-2=225$ mm., and at $3_1-3=177$ mm. The velocity is greatest at the end of inspiration and the beginning of expiration. Asphyxia increases it at first. Paralysis of the sympathetic increases it, while stimulation of this nerve diminishes it. Section of the vagi increases the velocity, while their stimulation of course diminishes it.

90. VELOCITY OF THE BLOOD.—(1) **Division of Vessels.—Arteries.**—In estimating the velocity of the blood, it is important to remember that the sectional area of all the branches of the aorta becomes greater as we proceed from the aorta towards the capillaries, so that the capillary area is 700 times greater than the sectional area of the aorta. As the veins join and form larger trunks, the venous area gradually becomes smaller, but the sectional area of the venous orifices at the heart is greater than that of the corresponding arterial orifices. [We may represent the result as two cones placed base to base (fig. 129), the bases meeting in the capillary area. The sectional area of the venous orifice (V) is represented larger than that of the arterial (A). The **increased sectional area** influences the **velocity** of the blood-current, while the resistance affects the pressure.]

(2) **Sectional Area.**—An equal quantity of blood must pass through every section

of the circulatory system, through the pulmonic as well as through the systemic circulation, so that the same amount of blood must pass through the pulmonary artery and aorta, notwithstanding the very unequal blood-pressure in these two vessels.

(3) **Lumen or Sectional Area.**—The velocity of the current, therefore, in various sections of the vessels, must be inversely as their sectional area.

(4) **Capillaries.**—Hence the velocity must diminish very considerably as we pass from the root of the aorta and the pulmonary artery towards the capillaries, so that the **velocity in the capillaries** of mammals = 0·8 millimetre per sec. ; frog = 0·53 ; man = 0·6 to 0·9 mm. [average 2 inches per minute]. According to A. W. Volkmann, the blood in mammalian capillaries flows 500 times slower than the blood in the aorta, so that the total sectional area of all the capillaries must be 500 times greater than that of the aorta. Donders found the velocity of the stream in the small afferent arteries to be 10 times faster than in the capillaries.

Veins.—The current becomes accelerated in the veins, but in the larger trunks it is 0·5 to 0·75 times less than in the corresponding arteries.

(5) **Mean Blood-Pressure.**—The velocity of the blood does not depend upon the *mean* blood-pressure, so that it may be the same in congested and in anæmic parts.

(6) **Difference of Pressure.**—On the other hand, the velocity in any section of a vessel is dependent on the difference of the pressure which exists at the commencement and at the end of that particular section of a blood-vessel ; it depends, therefore, on (1) the *vis a tergo* (i.e., the action of the heart), and (2) on the amount of the resistance at the periphery (dilatation or contraction of the small vessels).

Corresponding to the smaller difference in the arterial and venous pressure in the fœtus (§ 85), the velocity of the blood is less in this case (Cohnstein and Zuntz).

(7) **Pulsatory Acceleration.**—With *every pulse-beat* a corresponding acceleration of the blood-current (as well as of the blood-pressure) takes place in the arteries (pp. 144, 151). In large vessels Vierordt found the increase of the velocity during the systole to be greater by $\frac{1}{4}$ to $\frac{1}{2}$ than the velocity during the diastole. The variations in the velocity caused by the heart-beat are recorded in fig. 127, III, obtained by Chauveau's dromograph from the carotid of a horse. The velocity curve corresponds with a sphygmogram—P represents the primary elevation and R the dicrotic wave. This acceleration, as well as the pulse, disappears in the capillaries. A pulsatory acceleration, more rapid during its first phase, is observable in the small arteries, although the arteries themselves are not distended thereby.

(8) **Respiratory Effect.**—Every *inspiration retards* the velocity in the arteries, every *expiration aids* it somewhat ; but the value of these agencies is very small.

If we compare what has already been said regarding the effect of the respiration on the contraction and dilatation of the heart and on the blood-stream (§ 60), it is clear that **respiration favours the blood-stream**, and so does artificial respiration. When artificial respiration is interrupted, the blood-stream becomes slower (*Dogiel*). If the suspension of respiration lasts somewhat longer, the current is again accelerated on account of the dyspnoic stimulation of the vaso-motor centre (*Heidenhain*) (§ 371, 1.).

(9) **Modifying Conditions.**—Many circumstances affect the velocity of the blood in the veins. There are *regular* variations in the large veins near the heart

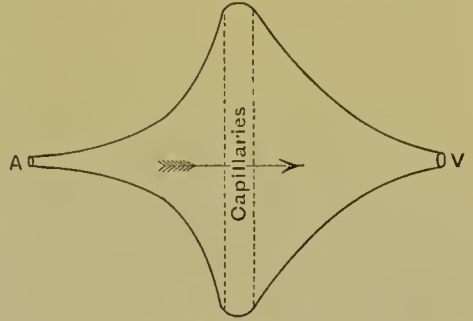


Fig. 129.

Scheme of the sectional area. A, arterial, and V, venous orifice. The common iliacs are an exception ; the sum of their sectional areas is less than that of the aorta ; the sections of the four pulmonary veins are together less than that of the pulmonary artery.

due to the *respiration and the movements of the heart* (§§ 50 and 60). (2) *Irregular variations* due to *pressure*, *e.g.*, from contracting muscles (§ 87), *friction* on the skin in the direction or against the direction of the venous current; the *position* of a limb or of the body. The pump-like action of the veins of the groin on moving the leg has been referred to (§ 87). When the lower limb is extended and rotated outwards, the femoral vein in the iliac fossa collapses, owing to an internal negative pressure; when the thigh is flexed and raised, it fills under a positive pressure (*Braune*). A similar condition obtains in walking.

91. CAPACITY OF THE VENTRICLES.—Vierordt calculated the capacity of the left ventricle from the velocity of the blood-stream, and the amount of blood discharged per second by the right carotid, right subclavian, the two coronary arteries, and the aorta below the origin of the innominate artery. He estimated that with every systole of the heart, 172 cubic centimetres (equal to 180 grams) of blood were discharged into the aorta; this, therefore, must be the capacity of the left ventricle (compare § 83).

92. THE DURATION OF THE CIRCULATION.—The time required by the blood to make a **complete circuit** through the course of the circulation was first determined by Hering (1829) in the horse. He injected a 2 per cent. solution of potassium ferrocyanide into a special vein, and ascertained (by means of ferric chloride) when this substance appeared in the blood taken from the corresponding vein on the *opposite* side of the body. The ferrocyanide may also be injected into the central or cardiac end of the jugular vein, and the time noted at which its presence is detected in the blood of the peripheral end of the same vein. Vierordt (1858) improved this method by placing under the corresponding vein of the opposite side a rotating disc, on which was fixed a number of cups at regular intervals. The first appearance of the potassium ferrocyanide is detected by adding ferric chloride to the serum which separates from the samples of blood after they have stood for a time. The duration of the circulation is as follows:—

Horse, . . . 31·5 seconds.	Hedgehog, . . 7·61 seconds.	Duck, . . . 10·64 seconds.
Dog, . . . 16·7 „	Cat, . . . 6·69 „	Buzzard, . . 6·73 „
Rabbit, . . . 7·79 „	Goose, . . . 10·86 „	Fowl, . . . 5·17 „

Results.—When these numbers are compared with the frequency of the normal pulse-beat in the corresponding animals, the following deductions are obtained:—

(1) The mean time required for the circulation is accomplished during 27 heart-beats, *i.e.*, for man = 32·2 seconds, supposing the heart to beat 72 times per minute.

(2) Generally, the mean time for the circulation in two warm-blooded animals is inversely as the frequency of the pulse-beats.

Modifying Conditions.—The time is influenced by the following factors:—

1. **Long vascular channels** (*e.g.*, from the metatarsal vein of one foot to the other foot) require a longer time than short channels (as between the jugulars). The difference may be equal to 10 per cent. of the time required to complete the entire circuit.

2. In **young animals** (with shorter vascular channels and higher pulse-rate) the time is shorter than in old animals.

3. **Rapid and energetic cardiac contractions** (as during muscular exercise) diminish the time. Hence rapid and at the same time less energetic contractions (as after section of both vagi), and slow but vigorous systoles (*e.g.*, after slight stimulation of the vagus) have no effect.

C. Vierordt estimated the **quantity of blood** in a man in the following manner:—In all warm-blooded animals, 27 systoles correspond to the time for completing the circulation. Hence, the total mass of the blood must be equal to 27 times the capacity of the ventricle, *i.e.*, in man, 187·5 grms. $\times$ 27 = 5062·5 grms. This is equal to $\frac{1}{13}$ of the body-weight in a person weighing 65·8 kilos. (compare § 40).

It is not to be forgotten that the salt used is to some extent poisonous, but Hermann uses the corresponding innocuous soda salt (25 per cent.).

Pathological.—The duration of the circulation seems to be increased during septic fever (*E. Wolff*).

93. WORK OF THE HEART.—The left ventricle expels 0·188 kilo. of blood with each systole, and in doing so it overcomes the pressure in the aorta, which is

equal to a column of blood 3.21 metres in height. [The amount of blood expelled from each ventricle during the systole is about 188 grms. (6 oz.). It is forced out against a pressure of 250 mm. Hg. = 3.21 metres of blood.] The work of the heart at each systole is $0.188 \times 3.21 = 0.604$ kilogram-metre. If the number of beats = 75 per minute, then the work of the left ventricle in 24 hours = $(0.604 \times 75 \times 60 \times 24) = 65,230$ kilogram-metres; while the "work" done by the *right* ventricle is about one-third that of the left, and therefore = 21,740 kilogram-metres. Both ventricles do work equal to 86,970 kilogram-metres. A workman during eight hours produces 300,000 kilogram-metres, *i.e.*, about four times as much as the heart. As the whole of the work of the heart is consumed in overcoming the resistance within the circulation, or rather is converted into heat, the body must be partly warmed thereby—(425.5 gram-metres are equal to 1 heat-unit, *i.e.*, the force required to raise 425.5 grams to the height of 1 metre may be made to raise the temperature of 1 cubic centimetre of water 1° C.). So that 204,000 "heat-units" are obtained from the transformation of the daily kinetic energy of the heart.

One gram of coal when burned yields 8080 heat-units, so that the heart yields as much energy per day for heating the body as if about 25 grams of coal were burned within it to produce heat.

94. BLOOD-CURRENT IN THE SMALLER VESSELS.—Methods.—The most important observations for this purpose are made by means of the **microscope** on transparent parts of living animals. Malpighi was the first to observe the circulation in this way in the lung of a frog (1661).

The following parts have been employed: The tails of tadpoles and small fishes; the web; tongue, mesentery, and lungs of eurydice frogs; the wing of the bat; the third eyelid of the pigeon or fowl; the mesentery; the vessels of the liver of frogs and newts, pia mater of rabbits, the skin on the belly of the frog, the mucous membrane of the inner surface of the human lip (*Hüter's* Cheilangioscope, 1879); the conjunctiva of the eyeball and eyelids. All these may be examined by *reflected* light.

[**Holmgren's Method.**—In studying the circulation in the frog's lung, it must be inflated. A cannula with a bulge on its free end is placed in the larynx, while to the other end is fixed a piece of caoutchouc tubing. The lung is inflated and then the caoutchouc tube is closed, after which the lung is placed in a chamber with glass above and below, and examined microscopically.]

[**Entoptical appearances** of the circulation (*Purkinje*, 1815). Under certain conditions a person may detect the movement of the blood-corpuscles within the blood-vessels of his own eye. The best method is that of Rood, *viz.*, to look at the sky through a dark blue glass, or through several pieces of cobalt glass placed over each other (*Helmholtz*).]

Form and Arrangement of Capillaries.—Regarding the form and arrangement of the capillaries, we find that—

1. The **diameter** which, in the finest, permits only the passage of single corpuscles in a row—one behind the other—may vary from 5μ to 20μ , so that two or more corpuscles may move abreast when the capillary is at its widest. [The capillaries are relatively wide in the lungs, and narrow in the brain, retina, and liver.]

2. The **length** is about 0.5 mm. They terminate in small veins.

3. The **number** is very variable, and the capillaries are most numerous in those tissues where the metabolism is most active, as in the lungs, liver, muscles—less numerous where the metabolism is slight, as in the sclerotic and in the nerve-trunks. [Many tissues are devoid of blood-vessels, *e.g.*, the cornea, nails, hairs.]

4. They form numerous **anastomoses**, and give rise to **networks**, whose form and arrangement are largely determined by the arrangement of the tissue elements themselves. They form *simple loops* in the skin, and polygonal networks in the serous membranes, and on the surface of many gland tubes; they occur in the form of elongated networks, with short connecting branches in muscle and nerve, as well as between the straight tubules of the kidney; they converge *radially* towards a central point in the lobules of the liver, and form *arches* in the free margins of the iris, and on the limit of the sclerotic and cornea.

[**Direct Termination of Arteries in Veins.**—Arteries sometimes terminate directly in veins, without the intervention of capillaries, *e.g.*, in the ear of the rabbit, in the terminal phalanges of the fingers and toes in man and some animals, in the cavernous tissue of the penis. They may be regarded as secondary channels which protect the circulation of adjacent parts, and they may also be related to the heat-regulating mechanisms of peripheral parts (*Hoyer*).]

In connection with the termination of arteries in capillaries, it is important to ascertain if the arterioles are **terminal arteries**, *i.e.*, if they do not form any further anastomoses with other similar arterioles, but terminate directly in capillaries, and thus only communicate by capillaries with neighbouring arterioles—or the arteries may anastomose with other arteries just before they break up into capillaries. This distinction is important in connection with the nutrition of parts supplied by such arteries (*Cohnheim*).

Capillary Circulation.—On observing the capillary circulation, we notice that the **red corpuscles** move only in the axis of the current (**axial current**), while the lateral transparent plasma-current flowing on each side of this central thread is free from these corpuscles. [The axial current is the more rapid.] This plasma layer or "**Poiseuille's space**" is seen in the smallest arteries and veins, where $\frac{2}{5}$ are taken up with the axial current, and the plasma layer occupies $\frac{1}{5}$ on each side of it (fig. 130). A great many, but not all, of the colourless corpuscles move in this layer. It is much less distinct in the capillaries. Rud. Wagner stated that it is absent in the finest vessels of the lung and gills [although Gunning was unable to confirm this statement]. The coloured corpuscles move in the smallest capillaries in *single file* one after the other; in the larger vessels, several corpuscles may move abreast, with a *gliding* motion, and in their course they may turn over and even be twisted if any obstruction is offered to the blood-stream. As a general rule, in these vessels the movement is uniform, but at a sharp bend of the vessel it may partly be retarded and partly accelerated. Where a vessel divides, not unfrequently a corpuscle remains upon the projecting angle of the division, and is doubled over it so that its ends project into the two branches of the tube. There it may remain for a time, until it is dislodged, when it soon regains its original form on account of its elasticity. Not unfrequently we see a red corpuscle becoming bent where two vessels meet, but on all occasions it rapidly regains its original form. This is a good proof of the elasticity of the coloured corpuscles. The motion of the **colourless corpuscles** is quite different in character; they *roll* directly on the *vascular wall*, moistened on their peripheral zone by the plasma in Poiseuille's space, their other surface being in contact with the thread of coloured corpuscles in the centre of the stream. Schklarewsky (1868) has shown by physical experiments that the particles of least specific gravity in all capillaries (*e.g.*, of glass) are pressed toward the wall, while those of greater specific gravity remain in the middle of the stream. [Graphite and particles of carmine were suspended in water, and caused to circulate through capillary tubes placed under a microscope, when the graphite kept the centre of the stream, and the carmine moved in the layer next the wall of the tube.]

When the colourless corpuscles reach the wall of the vessel, they must roll along, partly on account of their surface being *sticky*, whereby they readily adhere to the vessel, and partly because one surface is directed towards the axis of the vessel where the movement is most rapid, and where they receive impulses directly from the rapidly moving coloured blood-corpuscles (*Donders*). The rolling motion is not always uniform; not unfrequently it is retrograde in direction, which seems to be due to an irregular adherence to the vascular wall. Their *slower* movement (10 to 12 times slower than the red corpuscles) is partly due to their stickiness, and partly to the fact that, as they are placed near the wall, a large part of their surface lies in the peripheral threads of the fluid, which of course move more slowly (in fact, the layer of fluid next the wall is passive—p. 104).

[D. J. Hamilton finds that when a frog's web is examined in a vertical position, by far the greater proportion of leucocytes float on the *upper* surface, and only a few on the lower surface, of a small blood-vessel. In experiments to determine why the coloured corpuscles float or glide exclusively in the axial stream, while a great many, but not all, of the leucocytes roll in the peripheral layers, Hamilton ascertained that the nearer the suspended body approaches to the specific gravity of the liquid in which it is immersed, the more it tends to occupy the centre of the stream. He is of opinion that the phenomenon of the separation of the blood-corpuscles in the circulating fluid is due to the colourless corpuscles being specifically lighter, and the coloured

either of the same or of very slightly greater specific gravity than the blood-plasma. Hamilton controverts the statement of Schiklarewsky, and he finds that it is the relative specific gravity of a body which ultimately determines its position in a tube. These experiments point to the immense importance of a due relation subsisting between the specific gravity of the blood-plasma and that of the corpuscles.]

In the vessels first formed in the incubated egg, as well as in young tadpoles, the movement of the blood from the heart occurs in jerks (*Spallanzani*, 1768).

The velocity of the blood-stream is influenced by the *diameter of the vessels*, which undergo periodic changes of calibre. This change occurs not only in vessels provided with muscular fibres, but also in the capillaries, which vary in diameter, owing to the contraction of the cells composing their walls (p. 110).

The amount of *water in the blood* is of importance; when it is increased, the circulation is facilitated and accelerated (§ 62).

The velocity of the blood is greater in the **pulmonary** than in the systemic capillaries; so that the total sectional area of the pulmonary capillaries is less than that of all the systemic capillaries.

95. DIAPEDESIS.—If the circulation be studied in the vessels of the mesentery, we may observe **colourless corpuscles** passing out of the vessels in greater or less numbers (fig. 130). Mere contact with the air suffices to excite slight inflammation. At first the colourless corpuscles in the plasma-space move more slowly; several accumulate near each other, and adhere to the walls;—soon they bore into the wall, ultimately they pass quite through it, and may wander for a distance into the perivascular tissues. It is doubtful whether they pass through the so-called “*stomata*” which exist between the endothelial cells, or whether they simply pass through the cement substance between the endothelial cells (p. 108). This process is called **diapedesis**, and consists of several acts:—(a) The adhesion of colourless corpuscles to the inner surface of the vessel (after moving more slowly along the wall up to this point). (b) They send processes into and through the vascular wall. (c) The body of the cell is drawn after or follows the processes, whereby the corpuscle appears constricted in the centre (fig. 130, e). (d) The complete passage of the corpuscle through the wall, and its further motion in virtue of its own amoeboid movements. Hering observed that in large vessels with perivascular lymph-spaces, the corpuscles passed into the spaces, hence cells are found in lymph before it has passed through lymphatic glands. The **cause** of the diapedesis is partly due to the independent locomotion of the corpuscles, and it is partly a physical act, viz., a filtration of the colloid mass of the cell under the force of the blood-pressure (*Hering*)—in the latter respect depending upon the intra-vascular pressure and the velocity of the blood-stream. Hering regards this process, and even the passage of the coloured corpuscles through the vascular wall, as a normal process. The **red corpuscles** pass out of the vessels when the venous outflow is obstructed, which also causes the transudation of plasma through the vascular wall. The plasma carries the coloured corpuscles along with it, and at the moment of their passage through the wall they assume extraordinary shapes, owing to the tension put upon them, regaining their shape as soon as they pass out (*Cohnheim*). This remarkable phenomenon was described by Waller in 1846. It was redescribed by Cohnheim, and according to him the out-wandering is a sign of **inflammation**, and the colourless corpuscles which accumulate in the tissues are to be regarded as true **pus-corpuscles**, which may undergo further increase by division.

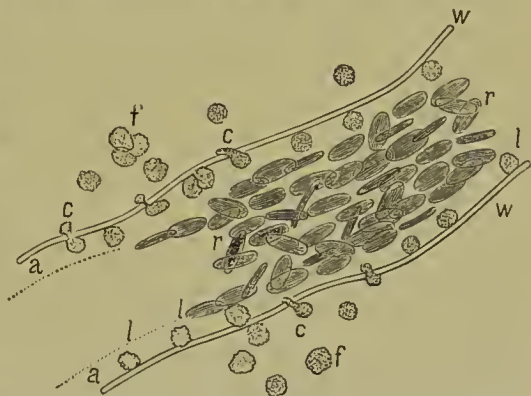


Fig. 130.

Small vessel of a frog's mesentery showing diapedesis. *w, w*, vascular walls; *a, a*, Poiseuille's space; *r, r*, red corpuscles; *l, l*, colourless corpuscles adhering to the wall, and *c, e*, in various stages of extrusion; *f, f*, extruded corpuscles.

Inflammation and Stasis.—When a strong stimulus acts on a vascular part, hyperæmic **redness** and **swelling** occur. Microscopic observation shows that the capillaries and the small vessels are dilated and *overfilled* with blood-corpuscles; in some cases, a temporary narrowing precedes the dilatation; simultaneously the velocity of the stream changes, rarely there is a temporary acceleration, *more frequently it becomes slower*. If the action of the stimulus or irritant be continued, the retardation becomes considerable, the stream moves in jerks, then follows a **to-and-fro movement** of the blood-column—a sign that stagnation has taken place in other vascular

areas. At last the blood-stream comes completely to a standstill—*stasis*—and the blood-vessels are plugged with blood-corpuscles. Numerous colourless blood-corpuscles are found in the stationary blood. Whilst these various processes are taking place, the colourless corpuscles—more rarely the red—pass out of the vessels. Under favourable circumstances the stasis may disappear. The swelling which occurs in the neighbourhood of inflamed parts is chiefly due to the *exudation* of plasma into the surrounding tissues.

96. MOVEMENT OF THE BLOOD IN THE VEINS.—In the smallest veins coming from the capillaries the blood-stream is more rapid than in the capillaries themselves, but less so than in the corresponding arteries. The stream is uniform, and if no other conditions interfered with it, the venous stream towards the heart ought to be uniform, but many circumstances affect the stream in different parts of its course. Amongst these are:—(1) The relative *laxness*, great *distensibility*, and the ready *compressibility* of the walls, even of the thickest veins. (2) The *incomplete filling* of the veins, which does not amount to any considerable distention of their walls. (3) The numerous and free *anastomoses* between adjoining veins, not only between veins lying in the same plane, but also between superficial and deep veins. Hence, if the course of the blood be obstructed in one direction, it readily finds another outlet. (4) The presence of numerous *valves* which permit the blood-stream to move only in a centripetal direction. They are absent from the smallest veins, and are most numerous in those of middle size.

Position of Valves.—The venous valves always have two pouches, and are placed at definite intervals, which correspond to the 1, 2, 3, or n^{th} power of a certain “fundamental distance,” which is = 7 mm. for the lower extremity and 5.5 mm. for the upper. Many of the original valves disappear. On the proximal side of every valve a lateral branch opens into the vein, while on the distal side of each branch lies a valve. The same is true for the lymphatics (*K. Bardleben*).

Effect of Pressure.—As soon as pressure is applied to the veins, the next lowest valves close, and those immediately above the seat of pressure open and allow the blood to move freely toward the heart. The *pressure* may be exerted from *without*, as by anything placed against the body; the thickened *contracted* muscles, especially the muscles of the limbs, compress the veins. That the blood flows out of a divided vein more rapidly when the muscles contract is shown during venesection. If the muscles are kept contracted, the venous blood passing out of the muscles collects in the passive parts, *e.g.*, in the cutaneous veins. The pulsatile pressure of the arteries accompanying the veins favours the venous current. From a hydrostatic point of view the valves are of considerable importance, as they serve to divide the column of blood into segments (*e.g.*, in the crural vein in the erect attitude), so that the fine blood-vessels in the foot are not subjected to the whole amount of the hydrostatic pressure in the veins.

The *velocity* of the venous blood has been measured directly (with the hæmadrometer and the rheometer—§ 89). Volkmann found it to be 225 mm. per sec. in the jugular vein. Reil observed that $2\frac{1}{2}$ times more blood flowed from an arterial orifice than from a venous orifice of the same size. The velocity of the venous current obviously depends upon the sectional area of the vessel. Borelli estimated the capacity of the venous system to be 4 times greater than that of the arterial; while, according to Haller, the ratio is 9 to 4.

Large Veins.—As we proceed from the small veins towards the *venæ cavæ*, the sectional area of the veins, taken as a whole, becomes less, so that the *velocity of the current increases* in the same ratio. The velocity of the current in the *venæ cavæ* may be about half of that in the aorta (*Haller*). As the *pulmonary veins* are narrower than the pulmonary artery, the blood moves more rapidly in the former.

97. SOUNDS WITHIN ARTERIES.—The sounds produced within arteries are, speaking from a physical point of view, only noises or bruits. Still, following Skoda's lead, they are spoken of by physicians as “tones.” Clinically, there is no sharp distinction between “tones,” sounds, noises, or bruits. In four-fifths of all healthy men two sounds—corresponding in duration and other characters to the two heart-sounds—are heard in the carotid (*Conrad, Weil*).

Sometimes only the second heart-sound is distinguishable, as its place of origin is near to the carotid. They are not true arterial sounds, but are simply "**propagated heart-sounds.**" Sometimes the sound of the pulmonary artery can be heard in this way (*Weil, Bettelheim*). These murmurs, sounds, or bruits occur either *spontaneously*, or are produced by the *application of external pressure*, whereby the lumen of the vessel is diminished. Hence one distinguishes: (1) **Spontaneous Murmurs**, and (2) **Pressure Murmurs**.

Arterial Sounds or murmurs are readily produced by pressing upon a strong artery, *e.g.*, the crural in the inguinal region, so as to leave only a narrow passage for the blood ("**stenosal murmur**"). A fine blood-stream passes with great rapidity and force through this narrow part into a wider portion of the artery lying behind the point of compression. Thus arises the "pressure-stream" (*P. Niemeyer*), or the "**fluid vein**" ("*veine fluide*" of Chauveau). The particles of the fluid are thrown into rapid *oscillation*, and undergo *vibratory* movements, and by their movements produce the sound within the peripheral dilated portion of the tube. A sound is produced in the fluid by pressure (*Corrigan*). The sounds are not caused by vibrations of the vascular wall, as supposed by Bouillaud.

A murmur of this sort is the "**sub-clavicular murmur**" (*Roser*), occasionally heard during systole in the subclavian artery; it occurs when the two layers of the pleura adhere to the apex of the lung (especially in tubercular diseases of the lungs), whereby the subclavian artery undergoes a local constriction due to its being made tense and slightly curved (*Friedreich*). This result is indicated in a diminution or absence of the pulse-wave in the radial artery (*Weil*).

It is obvious that arterial murmurs will occur in the human body:—(a) When, owing to pathological conditions, the arterial tube is *dilated at one part*, into which the blood-current is forcibly poured from the normal narrow tube. Dilatations of this sort are called **aneurisms**, in which murmurs are generally audible. (b) When **pressure** is exerted *upon an artery*, *e.g.* by the pressure of the greatly enlarged arteries during pregnancy, or by a large tumour pressing upon a large artery.

Spontaneous Murmurs.—In cases where no source of external pressure is discoverable, and when no aneurism is present, the spontaneously occurring sounds are favoured, when at the moment of arterial rest (cardiac systole) the arterial walls are distended to the slightest extent, and when during the movement of the pulse (cardiac diastole) the tension is most rapid (*Traube, Weil*), *i.e.*, when the low systolic minimum tension of the arterial wall passes rapidly into the high maximum tension. This is especially the case in insufficiency of the aortic valves, in which case the sounds in the arteries are audible over a wide area. If the minimum tension of the arterial wall is relatively great, even during diastole, the sounds in the arteries are greatly diminished.

Arterial murmurs are **favoured** by—(1) Sufficient delicacy and elasticity of the arterial walls. (2) Diminished peripheral resistance, *e.g.*, an easy outflow of the fluid at the end of the stream. (3) Accelerated current in the vascular system generally. (4) A considerable difference of the pressure in the narrow and wide portions of the tube. (5) Large calibre of the arteries.

In normal pulsating arteries, sounds may be heard especially at an acute bend of the artery. Murmurs of this sort are loudest where several large arteries lie together; hence, during pregnancy, we hear the *uterine murmur*, or **placental bruit**, or *souffle* in the greatly dilated uterine arteries. It is much less distinct in the umbilical arteries of the cord (umbilical murmurs). Similar sounds are heard through the thin walls of the head of infants, and a murmur is sometimes heard in the enlarged spleen in ague (*Maissurianz*).

Auscultation of the Normal Pulse.—On auscultating the radial artery under favourable circumstances, and especially in old thin persons with wide arteries and diastolic pulse, one may hear two sounds corresponding to the primary and diastolic waves.

In **insufficiency of the aortic valves**, characteristic sounds may be heard in the crural artery. If pressure be exerted upon the artery, a double blowing murmur is heard; the first one is due to a large mass of blood being propelled into the artery synchronously with the heart-beat, the second to the fact that a large quantity of blood flows back into the heart during diastole. If no pressure be exercised two sounds are heard, and these seem to be due to a wave propagated into the arteries by the auricles and ventricles respectively—compare § 73, fig. 94, III. In atheroma a double sound may sometimes be heard (§ 73, 2).

98. VENOUS MURMURS.—I. **Bruit de Diable.**—This sound is heard above the clavicles in the furrow between the two heads of the sterno-mastoid, most

frequently on the right side, and in 40 per cent. of all persons examined. It is either a continuous or a rhythmical murmur, occurring during the diastole of the heart or during inspiration; it has a whistling or rushing character, or even a musical quality, and arises within the bulb of the common jugular vein. When this sound is heard without pressure being exerted by the stethoscope, it is a pathological phenomenon. If, however, pressure be exerted, and if, at the same time, the person examined turn his head to the opposite side, a similar sound is heard in nearly all cases. The pathological *bruit de diable* occurs especially in anæmic persons, in lead-poisoning, in syphilitic and scrofulous persons, sometimes in young persons, and less frequently in elderly people. Sometimes a *thrill* of the vascular wall may be felt.

Causes.—It is due to the vibration of the blood flowing in from the relatively narrow part of the common jugular vein into the wide bulbous portion of the vessel, and seems to occur chiefly when the walls of a thin part of the vein lie close to each other, so that the current must purl through it. It is clear that pressure from without, or lateral pressure, as by turning the head to the opposite side, must favour its occurrence. Its *intensity* will be increased when the velocity of the stream is increased, hence *inspiration* and the *diastolic* action of the heart (both of which assist the venous current) increase it. The erect attitude acts in a similar manner. A similar bruit is sometimes, though rarely, heard in the subclavian, axillary, thyroid, facial, innominate and crural veins, and superior cava.

II. Regurgitant Murmurs.—On making a sudden effort, a murmur may be heard in the crural vein during expiration, which is caused by a centrifugal current of blood, owing to the incompetence or absence of the valves in this region. If the valves at the jugular bulb are not tight, there may be a bruit with expiration (*expiratory* jugular vein bruit—*Hamernik*), or during the cardiac systole (*systolic* jugular vein bruit—*v. Bamberger*).

III. Valvular Sounds in Veins.—When the tricuspid valve is incompetent during the ventricular systole, a large volume of blood is propelled backwards into the venæ cavæ. The venous valves are closed suddenly thereby and a sound produced. This occurs at the bulb or dilatation on the jugular vein (*v. Bamberger*), and in the crural vein at the groin (*N. Friedreich*), *i.e.*, only as long as the valves are competent. Forced expiration may cause a valvular sound in the crural vein. No sound is heard in the veins under perfectly normal circumstances.

99. THE VENOUS PULSE—PHLEBOGRAM.—**Methods.**—A tracing of the movements of a vein, taken with a lightly weighted sphygmograph, has a characteristic form, and is called a **phlebogram** (fig. 131). In order to interpret the various events of the phlebogram it is most important to record simultaneously the events that take place in the heart. The auricular contraction (compare fig. 47) is synchronous with *ab*; *bc*, with the ventricular systole, during which time the first sound occurs, whilst *a b* is a presystolic movement. The carotid pulse coincides nearly with the apex of the cardiogram, *i.e.*, almost simultaneously with the descending limb of the phlebogram (*Riegel*).

Occasionally in healthy individuals a pulsatile movement, synchronous with the action of the heart, may be observed in the common jugular vein. It is either confined to the lower part of the vein, the so-called bulb, or extends farther up along the trunk of the vein. In the latter case, the valves above the bulb are insufficient, which is by no means rare, even in health. The wave-motion passes from below upwards, and is most obvious when the person is in the passive horizontal position, and it is more frequent on the right side, because the right vein lies nearer the heart than the left. It is propagated more slowly than the arterial pulse-wave. The venous pulse resembles very closely the tracing of the cardiac impulse. Compare fig. 131, 1, with fig. 47.

It is obvious that, as the jugular vein is in direct communication with the right auricle, and as the pressure within it is low, the systole of the right auricle must cause a positive wave to be propagated towards the peripheral end of the jugular vein. Fig. 131, 9 and 10, are venous pulse-tracings of a healthy person with insufficiency of the valves of the jugular vein. In these curves the part *a b* corresponds to the contraction of the auricle. Occasionally this part consists of

two elevations, corresponding to the contraction of the atrium and auricle respectively. As the blood in the right auricle receives an impulse from the sudden tension of the tricuspid valve, *synchronous with the systole of the right ventricle*, there is a positive wave in the jugular vein in fig. 131, 9 and 10, indicated by *b, c*. Lastly, the sudden closure of the pulmonary valves may even be indicated (*e*). As the aorta lies in direct relation with the pulmonary artery, the sudden closure of its valves may also be indicated (fig. 131, 9 at *d*). During the diastole of the auricle and ventricle, blood flows into the heart, so that the vein partly collapses and the lever of the recording instrument descends.

Sinus and Retinal Pulse.—The blood in the sinuses of the *brain* also undergoes a pulsatile movement, owing to the fact that during cardiac diastole much blood flows into the veins (*Mosso*). Under favourable circumstances, this movement may be propagated into the veins of the *retina*, constituting the *venous retinal pulse* of the older observers (*Helfreich*).

Pathological Jugular Vein Pulse.—The venous pulse in the jugular vein is far better marked in *insufficiency of the tricuspid valve*, and the vein may pulsate violently, but if its valves be

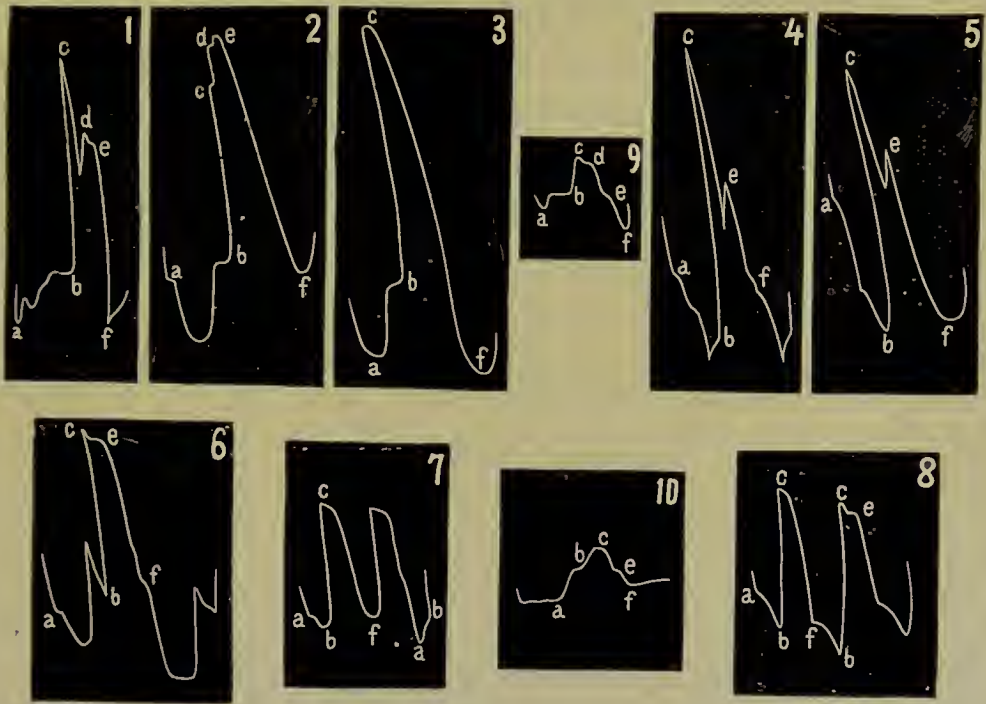


Fig. 131.

Venous pulses (*Friedreich*). 1-8, from insufficiency of the tricuspid ; 9, 10, pulse of the jugular vein of a healthy person. In all the curves, *a b*=contraction of the right auricle ; *b c*, of the right ventricle ; *d*, closure of the aortic valves ; *e*, closure of the pulmonary valves ; *e f*, diastole of the right ventricle.

perfect, the pulse is not propagated along the vein, so that *a pulse in the jugular vein is not necessarily a sign of insufficiency of the tricuspid valve*, but only of insufficiency of the valve of the jugular vein (*Friedreich*).

Liver Pulse.—The ventricular systole is propagated into the valveless inferior vena cava, and causes the *liver pulse*. With each systole blood passes into the hepatic veins, so that the liver undergoes a *systolic swelling and injection*.

Fig. 131, 2-8, are curves of the pulse in the common jugular vein. Although at first sight the curves appear to be very different, they all agree in this, that the various events occurring in the heart during a cardiac revolution are indicated more or less completely. In all the curves, *a b*=auricular contraction. The auricle, when it contracts, excites a positive wave in the veins. The elevation, *b c*, is caused by the large blood-wave produced in the veins, owing to the emptying of the ventricle. It is always greater, of course, in insufficiency of the tricuspid valves than under normal circumstances (fig. 131, 9 and 10). In the latter case, the closure of the tricuspid valve causes only a slight wave-motion in the auricle. The apex, *c*, of this wave

may be higher or lower, according to the tension in the vein and the pressure exerted by the sphygmograph. As a general rule, at least one notch (4, 5, 6, *e*) follows the apex, due to the prompt closure of the valves of the pulmonary artery. The closure of the closely adjacent aortic valves may cause a small secondary wave near to *e* (as in 1 and 2, *d*). The curve falls towards *f*, corresponding to the diastole of the heart.

A well-marked venous pulse occurs when the *right auricle is greatly congested*, as in cases of insufficiency of the mitral valve or stenosis of the same orifice. In rare cases, in addition to the pulse in the common jugular vein, the external jugular, the facial, thyroid, external thoracic veins, or even the veins of the upper and lower extremities may pulsate. A similar pulsation must occur in the pulmonary veins in mitral insufficiency, but of course the result is not visible.

On rare occasions a pulse occurs in the veins on the back of the hand and foot, owing to the arterial pulse being propagated through the capillaries into the veins. This may occur under normal circumstances, when the peripheral ends of the arteries become dilated and relaxed (*Quincke*), or when the blood-pressure within these vessels rises rapidly and falls as suddenly, as in **insufficiency of the aortic valves**. [Venous pulse in submaxillary vein (p. 135)].

In progressive effusion into the pericardium, the carotid pulse at first becomes smaller and the venous pulse larger; beyond a certain stage of pressure the latter ceases (*Riegel*).

100. DISTRIBUTION OF THE BLOOD.—In the rabbit, one-fourth of the total amount of the blood is found in each of the following:—*a*, in the passive muscles; *b*, in the liver; *c*, in the organs of the circulation (heart and great vessels); *d*, in all other parts together.

Methods.—The methods adopted do not give exact results. J. Ranke ligatured the parts during life, removed them, and investigated the amount of blood while the tissues are still warm.

Influencing Conditions.—The amount of blood is influenced by—(1) the anatomical distribution of the vessels (vascularity or the reverse) as a whole; (2) the diameter of the vessels, which depends upon physiological causes—(*a*) on the blood-pressure within the vessels; (*b*) on the condition of the vaso-motor or vaso-dilator nerves; (*c*) on the condition of the tissues in which the blood-vessels are distributed, *e.g.*, the vessels of the intestine during absorption; the vessels of muscle during muscular contraction; and the vessels in inflamed parts.

The most important factor, however, is the state of **activity of the organ itself**; hence the saying, “ubi irritatio, ibi affluxus.” We may instance the congestion of the salivary glands and the gastric mucous membrane during digestion, and the increased vascularity of muscles during contraction. As the activity of organs varies at different times, the *amount of blood in the part or organ goes hand in hand with the variations in its states of activity*. When some organs are congested, others are at rest; during digestion there is muscular relaxation and less mental activity: violent muscular exertion retards digestion—during great congestion of the cutaneous vessels the activity of the kidneys diminishes. Many organs (heart, muscles of respiration, certain nerve-centres) seem always to be in a nearly uniform state of activity and vascularity. During the *activity of an organ*, the amount of blood in it may be increased 30 per cent., nay, even 47 per cent. The motor organs of young muscular persons are relatively more vascular than those of old and feeble persons (*J. Ranke*). In the condition of increased activity, a *more rapid renewal* of the blood seems to occur; after muscular exertion the duration of the circulation diminishes (*Vierordt*).

During a condition of mental activity, the carotid is dilated, the diastolic wave in the carotid curve is increased (the radial shows the opposite condition), and the pulse is increased in frequency (*Gley*).

Age.—The *development of the heart and large vessels* determines a different distribution of the blood in the child from that which obtains in the adult. The heart is relatively small from infancy up to puberty, the vessels are relatively large; while after puberty the heart is large, and the vessels are relatively smaller. Hence it follows that the blood-pressure in the arteries of the systemic circulation must be lower in the child than in the adult. The pulmonary artery is relatively wide in the child, while the aorta is relatively small; after puberty both vessels have nearly the same size. Hence it follows that the blood-pressure in the pulmonary vessels of the child is relatively higher than that in the adult (*Bencke*).

101. PLETHYSMOGRAPHY.—In order to estimate and register the amount of blood in a limb Mosso devised the **plethysmograph** (fig. 132).

It consists of a long cylindrical glass vessel, G, suited to accommodate a limb. The opening through which the limb is introduced is closed with caoutchouc, and the vessel is filled with water. There is an opening in the side of the vessel in which a manometer tube, filled to a certain height with water, is fixed. As the arm is enlarged owing to the increased supply of arterial blood passing into it at each pulse-beat, of course the water column in the manometer

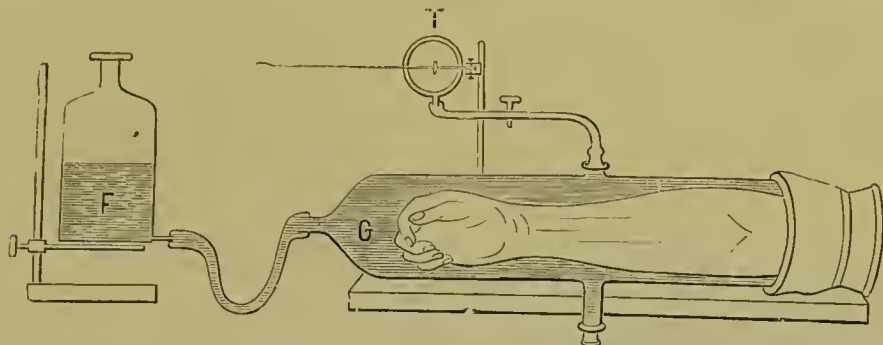


Fig. 132.

Mosso's plethysmograph. G, glass vessel for holding a limb; F, flask for varying the water-pressure in G; T, recording apparatus.

is raised. Fick placed a float upon the surface of the water, and thus enabled the variations in the volume of the fluid to be inscribed on a revolving cylinder. The curve obtained resembled the pulse-curve; it was even dicrotic. In fig. 132 the movement of the fluid is represented as conveyed to a Marey's tambour, T, similar to the recording apparatus employed in Brondgeest's pansphygmograph (fig. 88).

The cylinder G may be filled with air. Kries fills it with gas and connects the tube leading to T to a gas-burner. The variations in the gas-flame are then photographed. RECEIVED

Results.—(1) **Pulsatile Variations in the Volume.**—As the venous current is regarded as uniform in the passive limb, every increase of the volume-curve indicates a greater velocity of the arterial current towards the periphery, and *vice versa* (Fick). The curves registered by the apparatus are **volume pulses**, and they resemble the curve of the dromograph (fig. 127, III). The ascent of the curve indicates a greater, the descent a diminished inflow of arterial blood.

At first sight the plethysmograph curve (volume-pulse, § 90, 7) is very like the pulse-curve (pressure pulse); both are dicrotic. But there are differences; the volume pulse-curve beyond the apex falls more rapidly. This rapid fall, which is not accompanied by a corresponding fall of the pressure, is attributed by v. Kries to peripheral reflexion. The dicrotic wave occurs sooner in the volume-pulse than in the pulse-curve.

(2) The **respiratory undulations** correspond to similar variations in the blood-pressure tracing (§ 85, f). Vigorous respiration and cessation of the respiration cause a diminution of the volume. The limb swells during straining and coughing, but diminishes during sighing. (3) Certain **periodic undulations** occur, due to the regular periodic contractions of the small arteries. (4) Other undulations, due to various accidental causes, affect the blood-pressure: changes of the position of a limb acting hydrostatically, and dilatation or contraction of the vessels in other vascular regions. (5) Movement of the muscles of the limb under observation causes diminution of volume, as the venous current is accelerated, the musculature is also very slightly diminished in volume, even when the intra-muscular vessels are dilated. (6) *Mental exercise* causes a diminution in the volume of the limb, and so does sleep (Mosso). *Music* influences the blood-pressure in dogs, the pressure rising or falling under different conditions. The state of excitement of the auditory nerve is transmitted to the medulla oblongata, where it acts so as to cause acceleration of the action of the heart (Dogiel). (7) *Compression of the afferent artery* causes a decrease, and *compression of the vein* an increase in the volume of the limb (Mosso). (8) Stimulation of the vaso-motor nerves causes a decrease, that of the vaso-dilators an increase in the volume (Bowditch and Warren).

102. TRANSFUSION OF BLOOD.—Transfusion is the introduction of blood from one animal into the vascular system of another animal.

(a) The **red corpuscles** are the most important elements in connection with the restorative powers of the blood. They seem to preserve their functions even in blood which has been defibrinated outside the body (§ 4, A).

(b) With regard to the **gases** present in the blood, arterial blood never acts injuriously; but venous blood overcharged with carbonic acid ought only to be transfused when the respiration is sufficient to oxygenate the blood as it passes through the pulmonary capillaries, whereby venous is transformed into arterial blood. If the respiratory movements have ceased, or are imperfectly performed, the blood becomes rapidly richer in carbonic acid, and in this condition reaches the heart; thence it is propelled into the blood-vessels of the medulla oblongata, where it acts as a powerful stimulus of the respiratory centre, causing dyspnoea, convulsions, and death.

(c) The **fibrin**, and the substances from which it is formed, do not seem to play any part in connection with the restorative powers of the blood; hence, defibrinated blood performs all the functions of non-defibrinated blood within the body (*Panum, Landois*).

(d) The investigations of Worm Müller showed that an **excess** of 83 per cent. of blood may be transfused into the vascular system of an animal (dog) without producing any injurious effects. Hence it follows that the vascular system has the power of accommodating large quantities of blood within it. That the vascular system can accommodate itself to a diminished amount of blood has been known for a long time (§ 85, c). It is very important to observe that the transfusion of a large quantity of blood does not materially or permanently raise the blood-pressure.

When Employed.—The transfusion of blood is used—(1) in **acute anæmia** (§ 41, 1), *e.g.*, after copious hæmorrhage. New blood (150 to 500 c.c.), from the *same species* of animal, is introduced directly into the vessels, to supply the place of the blood lost by the hæmorrhage.

(2) In cases of **poisoning**, where the blood has been rendered useless by being mixed with a poisoning substance, and hence is unable to support life. In such cases remove a considerable quantity of the blood, and replace it by fresh blood. Carbonic oxide is a poison of this kind, and its effects on the body have already been described (§ 16). A similar practice is indicated in poisoning with ether, chloral, chloroform, opium, morphia, strychnine, cobra poison, and such substances as dissolve the blood-corpuscles, *e.g.*, potassic chlorate.

(3) Under certain **pathological conditions** the blood may become so altered in quality as to be unable to support life. The morphological elements of the blood may be altered, and so may the relative proportion of its other constituents. Amongst these conditions may be cited the pathological condition of uræmia, due, it may be, to the accumulation of urea or the products of its decomposition within the blood; accumulation of the biliary constituents in the blood, and great increase of the carbonic acid. All these three conditions, when very pronounced, may cause death. In these cases, part of the impure blood may be replaced by normal human blood.

Amongst conditions where the **morphological constituents** of the blood are altered qualitatively or quantitatively are: hydræmia (excessive amount of water in the blood, § 41, 1); oligocythæmia (abnormal diminution of red blood-corpuscles). When these conditions are highly developed, more especially in pernicious anæmia (§ 10, 2), healthy blood may be substituted. Transfusion is not suited for persons suffering from leukæmia (compare p. 21).

After Effects.—A quarter or half an hour after normal blood has been injected into the blood-vessels of a man, there is a greater or less *febrile reaction*, according to the amount of blood transfused (Fever, § 220).

Operation.—The operative procedure to be adopted in the process of transfusion varies according as defibrinated or non-defibrinated blood is used. In order to defibrinate blood, some blood is withdrawn from a vein of a healthy man in the ordinary way, collected in an open vessel, and whipped or beaten with a glass rod until all the fibrin is completely removed from it. It is then filtered through an atlas filter, heated to the temperature of the body (by placing it in a vessel in warm water), and injected by means of a syringe into an artery opened for the purpose. A vein (*e.g.*, basilic or great saphenous) may be selected for the transfusion, in which case the blood is driven inward in the direction of the heart; if an artery is selected (radial or posterior tibial) the blood is injected towards the periphery, or towards the heart.

If non-defibrinated human blood is used, the blood may be passed *directly* from the arm of the giver to the arm of the receiver by means of a flexible tube. The tube used must be filled with normal saline solution to prevent the entrance of air. [J. Duncan collects the blood shed during an operation in a 5 per cent. solution of sodic phosphate (*Pavy*), and injects the mixture, especially where much blood has been lost previously.]

Dangers.—It is most important that no air be allowed to pass into the circulation, for if it be introduced in sufficient quantity it may cause death. When air enters the circulation it reaches the right side of the heart, where, owing to the movement of the blood, it forms air-bubbles and makes a froth. The air-bubbles are pumped into the branches of the pulmonary artery, in which they become impacted, arrest the pulmonary circulation, and rapidly cause death.

Peritoneal Transfusion.—Recently, the injection of defibrinated blood into the *peritoneal cavity* has been recommended. The blood so injected is absorbed (*Ponfick*). Even after twenty minutes the number of blood-corpuscles in the blood of the recipient (rabbit) is increased, and the number is greatest on the first or second day. The operation, however, may cause death, and one fatal case, owing to peritonitis, is recorded (*Mosler*). It is evident that this method of transfusion is not applicable in cases where blood must be introduced into the circulation as rapidly as possible (*e.g.*, after severe hæmorrhage or in certain cases of poisoning. [Blood has been injected into the subcutaneous cellular tissue of the abdomen in cases of great debility.]

Heterogeneous Blood.—*The blood of animals ought never to be transfused into the blood-vessels of man.* It is to be remembered, however, that the blood-corpuscles of the sheep are rapidly dissolved by human blood, so that the active constituents of the blood are rendered useless (*Landois*). As a general rule, the blood-serum of some mammals dissolves the blood-corpuscles of other mammals (§ 5, 5).

Solution of the Blood-Corpuscles.—The serum of dog's blood is a powerful solvent, while that of the blood of the horse and rabbit dissolves corpuscles relatively slowly. The blood-corpuscles of mammals vary very greatly with reference to their power to resist the solvent action of the serum of other animals. The red blood-corpuscles of rabbits' blood are rapidly dissolved by the blood-serum of other animals, whilst those of the cat and dog resist the solvent action much longer. Solution of the corpuscles occurs in defibrinated as well as in ordinary blood. When the blood of a rabbit or lamb is injected into the blood-vessels of a dog, the red blood-corpuscles are dissolved in a few minutes. If blood be withdrawn by pricking the skin with a needle, the partially dissolved corpuscles may be detected.

Liberation of Hæmoglobin and Hæmoglobinuria.—As a result of the solution of the coloured corpuscles, the blood-plasma is reddened by the liberated hæmoglobin. Part of the dissolved material may be used up in the body of the recipient, some of it for the formation of bile, but if the solution of the corpuscles has been extensive, the hæmoglobin is *excreted in the urine* (hæmoglobinuria), in less amount in the intestine, the bronchi, and the serous cavities. Bloody urine has been observed in man after the injection of 100 grains of lamb's blood. Even some of the recipient's blood-corpuscles are dissolved by the serum of the transfused blood, *e.g.*, on transfusing dog's blood into man. In the rabbit, whose corpuscles are readily dissolved, the transfusion of the *blood-serum* of the dog, man, pig, sheep, or cat produces serious symptoms, and even death. The dog, whose corpuscles are more resistant, bears transfusion of other kinds of blood well.

Dangers.—When *foreign* or *heterogeneous* blood (*i.e.*, blood from a different species) is transfused, two phenomena, which may be dangerous to life, occur:—

(1) Before the corpuscles are dissolved, they usually run together and form sticky masses, consisting of 10 or 12 corpuscles, which are apt to occlude the capillaries. After a time they give up their hæmoglobin, leaving the stroma, which yields a sticky fibrin-like mass that may occlude fine vessels (§ 31).

(2) The presence of a large quantity of dissolved hæmoglobin may cause extensive coagulation within the blood-vessels. The injection of dissolved hæmoglobin causes extensive coagulations (*Naunyn and Francken*).

The coagulation occurs usually in the venous system and in the larger vessels, and may cause death either suddenly or after a considerable time.

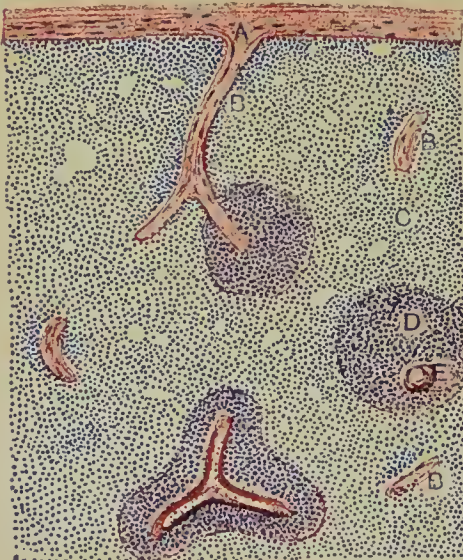
Dissolved hæmoglobin seems greatly to increase the activity of the fibrin-ferment (§ 30), perhaps by accelerating the disintegration of the colourless corpuscles. Hæmoglobin exposed to the air gradually loses this property; and the fibrin-ferment, when in contact with hæmoglobin, is either destroyed or rendered less active (*Sachssendahl*).

Vascular Symptoms.—As a result of the above-named causes of occlusion of the vessels, there are often signs of the circulation being impeded in various organs. In man, after transfusion of lamb's blood, the skin is bluish-red, in consequence of the stagnation of blood in the cutaneous vessels. Difficulty of breathing occurs from obstruction in the capillaries of the lung; while there may be rupture of small bronchial vessels, causing sanguineous expectoration. The dyspnea may increase, especially when the circulation through the medulla oblongata—the seat of the respiratory centre—is interfered with. In the digestive tract, for the same reason, *increased peristalsis*, evacuation of the contents of the rectum, vomiting, and abdominal pain may occur. These phenomena are explained by the fact that disturbances of the circulation in the intestinal vessels cause increased peristaltic movements. Degeneration of the parenchyma of the *kidney* occurs as a result of the occlusion of some of the renal vessels. The uriniferous tubules become plugged with cylinders of coagulated albumin (*Ponfick*). Owing to the occlusion of numerous small muscular branches, the *muscles* may become stiff, or coagulation of their myosin may occur. Other symptoms, referable to the *nervous system*, *sense-organs*, and *heart*, are all due to the interference with the circulation through them. An important symptom is the occurrence of a considerable amount of *fever* half an hour or so after the transfusion of heterogenous blood (§ 200). When many vessels are occluded, rupture of some small blood-vessels may take place. This explains the occurrence of slight, yet persistent hæmorrhages, which occur on the free surfaces of the mucous and serous membranes, and in the parenchyma of organs, as well as in wounds. The blood coagulates with difficulty, and imperfectly.

Transfusion of other Fluids.—Other substances have been transfused. **Normal saline solution** (0·6 per cent. NaCl), or **serum** from the same species, aids the circulation in a purely mechanical way (*Goltz*), and it even excites the circulation (*Kronecker*). In severe anemia this fluid cannot maintain life (*Eulenburg and Landois*). The injection of **peptone**, or rather the **albumoses**, even in moderate amount, is dangerous to life, as it causes paralysis of the vessels (p. 36).

The Blood Glands.

103.—I.—THE SPLEEN.—Structure.—The spleen is covered by the peritoneum, except at the hilum. Under this **serous** covering there is a tough, thick, elastic, fibrous **capsule**, which closely invests the organ and gives a



A, capsule; B, trabeculae; C, splenic pulp;
D, splenic corpuscle; E, artery.

Fig. 133.

Section of human spleen × 10 times.

covering to the vessels which enter or leave it at the hilum, so that fibrous tissue is carried into the organ along the course of the vessels (fig. 133). [The capsule cannot be separated without tearing the splenic pulp.] Numerous **trabeculae** pass into the spleen from the deep surface of the capsule, where they branch and anastomose so as to produce a network of sustentacular tissue, which is continuous with the connective-tissue, prolonged inwards and surrounding the blood-vessels (fig. 134). Thus, the connective-tissue in the spleen, as in other viscera, is continuous throughout the organ. In this way an irregular dense network is formed, comparable to the meshes of a bath sponge. [This network is easily demonstrated by washing out the pulp lying in its meshes by means of a stream of water, when a beautiful soft semi-elastic network or **framework** of rounded and flattened threads is obtained.] The **capsule** (fig. 133) is composed of interlacing bundles of connective-tissue mixed

with numerous fine fibres of elastic tissue and some non-striated fibres.

Reticulum.—Within the meshes of the trabecular framework there is disposed a very delicate network or reticulum of adenoid tissue, which, with the other

coloured elements that fill up the meshes, constitute the splenic pulp (fig. 135). The reticulum is continuous with the fibres of the trabeculae. [If a fine section of the spleen be "pencilled" in water, so as to remove the cellular elements, the preparation presents much the same characters as a section of a lymph-gland similarly treated, viz., a very fine network of adenoid tissue, continuous with, and surrounding the walls of, the blood-vessels. The spaces of this tissue are filled with lymph- and blood-corpuscles.]

The **pulp** is a dark reddish-coloured, semi-fluid material, which may be squeezed or washed out of the meshes in which it lies. It contains a large number of coloured blood-corpuscles, and becomes brighter when it is exposed to the action of the oxygen of the air.

Blood-Vessels and Malpighian Corpuscles.—The large splenic artery, accompanied by a vein, splits up into several branches before it enters the spleen. Both vessels and their branches are enclosed in a fibrous sheath, which becomes continuous with the trabeculae. The smaller branches of the artery gradually lose this fibrous investment, and each one ultimately divides into a group or pencil of arterioles or **penicilli** *which do not anastomose with each other*. [Thus each branch is **terminal**—a condition which is of great importance in connection with the pathology of embolism or infarction of the vessels of the spleen.] At the points of division of the branches of the artery, or scattered along their course, are small oval or globular masses of adenoid tissue ($\frac{1}{80}$ to $\frac{1}{20}$ inch in diameter), the **Malpighian corpuscles**. [These bodies are visible to the naked eye as small, round, or oval

white structures, about the size of millet seed, in a section of a fresh spleen. They are very numerous

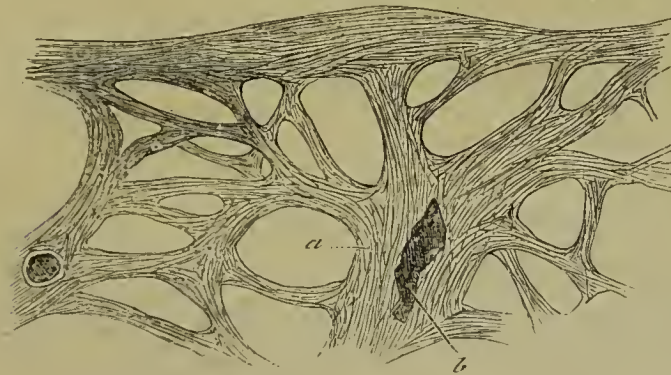


Fig. 134.

Trabeculae of the spleen of a cat with the splenic pulp washed out. *a*, trabecula; *b*, vein.

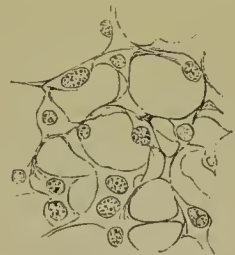


Fig. 135.

Adenoid reticulum of spleen of cat.

—[70,000 in man]—and are readily detected in the dark reddish pulp. One must be careful not to mistake sections of the trabeculae for them. These corpuscles consist of adenoid tissue, whose meshes are filled with lymph-corpuscles, and they present exactly the same structure as the solitary follicles of the intestine (§ 197). They are small lymphatic accumulations around the arteries—**peri-arterial masses of adenoid tissue** similar to those masses that occur in a slightly different form in other organs, *e.g.*, the lungs. In a section of the spleen the artery may pass through the centre of the mass or through one side of it, and in some cases the tissue is collected unequally on opposite sides of the vessel, so that it is lob-sided. They are not surrounded by any special envelope. In some animals the lymphatic tissue is continued for some distance along the small arteries, so that to some extent it resembles a peri-vascular sheath of adenoid tissue. In a well-injected spleen, a few fine capillaries are to be found within these corpuscles. The capillaries distributed in the substance of the Malpighian corpuscle (fig. 136) form a network, and ultimately pour their blood into the spaces in the pulp. According

to Cadiat, the corpuscles are separated from the splenic pulp by a lymphatic sinus, which is traversed by efferent capillaries passing to the pulp (fig. 136).

Connection of Arteries and Veins.—It is very difficult to determine what is the exact mode of termination of the arteries within the spleen, more especially as it is extremely difficult to inject the blood-vessels of the spleen. According to Stieda and others, the fine “capillary arteries” formed by the division of the small arteries do not open directly into the capillary veins, but the connection



Fig. 136.

Malpighian corpuscle of a cat's spleen injected. *a*, artery; *b*, meshes of the pulp injected; *c*, the artery of the corpuscle ramifying in the lymphatic tissue composing it.

between the arteries and veins is by means of the “intermediary inter-cellular spaces” of the reticulum of the spleen, so that, according to this view, there is no continuous channel lined throughout by epithelium connecting these vessels one with another. Thus the blood of the spleen flows into the spaces of the adenoid reticulum just as the lymph-stream flows through the spaces in a lymph-gland. According to Billroth and Kölliker, a closed blood-channel actually does exist between the capillary arteries and the veins, consisting of dilated spaces (similar to those of erectile tissue). These intermediary spaces are said to be completely lined by spindle-shaped epithelium, which abuts externally on the reticulum of the pulp. [According to Frey, owing to the walls of the terminal vessels being incomplete,

there being clefts or spaces between the cells composing them, the blood passes freely into spaces of the adenoid tissue of the pulp “in the same way as the water of a river finds its way amongst the pebbles of its bed,” these “intermediary passages” being bounded directly by the cells and fibres of the network of the pulp. From the passages the venous radicles arise. At first their walls are imperfect and cribriform, and they often present peculiar transverse markings, due to the circular disposition of the elastic fibres of the reticulum. The small veins have at first a different course from the arteries. They anastomose freely, but they soon become ensheathed, and accompany the arteries in their course.]



Fig. 137.

Elements of human splenic pulp. 1, colourless cells; 2, endothelium; 3, coloured blood-corpuscles; 4, cells containing granules, the upper one with a colourless blood-corpuscle *b*, enclosed in it.

Elements of the Pulp (fig. 137).—The morphological elements are very various—(1) Lymph-corpuscles of various sizes, sometimes partly swollen, and at other times with granular contents. (2) Red blood-corpuscles. (3) Transition forms between 1 and 2 [although this is denied by some observers (§ 7, C)]. (4) Cells containing red blood-corpuscles and pigment granules. [These cells exhibit amoeboid movements.] (Compare § 8.)

[**Lymphatics** undoubtedly arise within the spleen, but they are not numerous. There are two systems—a superficial or capsular, and trabecular system; and a peri-vascular set. The **superficial** lymphatics in the capsule are rather more numerous. Some of them seem to communicate with the lymphatics within the

organ (*Tomsa, Kölliker*). In the horse's spleen they communicate with the lymphatics in the trabeculæ, and with the peri-vascular lymphatics. The exact mode of origin of the **peri-vascular** system is unknown, but in part at least it begins in the spaces of the adenoid tissue of the Malpighian corpuscles and peri-vascular adenoid tissue, and runs along the arteries towards the hilum. There seem to be no afferent lymphatics in the spleen such as exist in a lymphatic gland.]

The **nerves** of the spleen are composed for the most part of non-medullated nerve-fibres, and run along with the artery. Their exact mode of termination is unknown, but they probably go to the blood-vessels and to the muscular tissue in the capsule and trabeculæ. [They are well seen in the spleen of the ox, and in their course very small ganglia, placed wide apart, have been found by Remak and W. Stirling.]

Chemical Composition.—Several of the more highly oxidised stages of albuminous bodies exist in the spleen. Besides the ordinary constituents of the blood, there exist:—leucin, tyrosin, xanthin, hypoxanthin; lactic, butyric, acetic, formic, succinic, and uric acids, and perhaps glyeero-phosphoric acid (*Salkowski*); cholesterin, a glutin-like body, inosit, a pigment containing iron, and even free iron oxide (*Nasse*). The ash is rich in phosphoric acid and iron (p. 170); poor in chlorine compounds. The splenic juice is alkaline in reaction; the specific gravity of the spleen = 1059–1066.

The **functions of the spleen** are obscure, but we know some facts on which to form a theory. [The spleen differs from other organs in that no very apparent effect is produced by it, so that we must determine its uses in the economy from a consideration of such facts as the following:—(1) The effects of its removal or extirpation. (2) The changes which the blood undergoes as it passes through it. (3) Its chemical composition. (4) The results of experiments upon it. (5) The effects of diseases.]

(1) **Extirpation.**—The spleen may be removed from an animal—old or young—without the organism suffering any very obvious change (*Galen*). The human spleen has been successfully removed by *Köberle, Péan*, and others. As a result (compensatory?) the lymphatic glands enlarge, but not constantly, while the blood-forming activity of the red marrow of bone is increased. Small brownish-red patches were observed in the intestines of frogs after extirpation of the spleen. These new formations are regarded by some observers as compensatory organs. *Tizzoni* asserts that new splenic structures are formed in the omentum (horse, dog) after the destruction of the parenchyma and blood-vessels of the spleen. The spleen is absent extremely seldom.

[The weight of the animal (dog) diminishes after the operation, but afterwards increases. The number of red blood-corpuscles is lessened, reaching its minimum about the 150th to the 200th day, while the colourless corpuscles are increased in number. The lymphatic glands (especially the internal, and those in the neck, mesentery, and groin) enlarge, while on section the cortical substance of these structures is redder, owing to the great number of red corpuscles; many of them are nucleated in the lymph spaces (*Gibson*). The marrow of all the long bones (those of the foot excepted) becomes very red and soft, with the characters of embryonic bone-marrow. Such animals withstand hæmorrhage (to $\frac{1}{3}$ of the total amount of blood) without any specially bad results (*Tizzoni, Winogradow*). *Schindeler* observed that animals after extirpation of the spleen became very ravenous.]

[**Regeneration.**—After entire removal of the spleen, nodules of splenic tissue are reproduced (fox); while new adenoid tissue is formed in the lymphatic glands, and in Peyer's patches, the parenchyma of the former coming to resemble splenic tissue (*Tizzoni, Eternod*).]

(2) According to *Gerlach* and *Funke* the spleen is a **blood-forming gland**. The blood of the splenic vein contains far more colourless corpuscles than the blood of the splenic artery (p. 53). Many of these corpuscles undergo fatty degeneration, and disappear in the blood-stream. That colourless blood-corpuscles are formed within the spleen seems to be proved by the enormous number of these corpuscles which are found in the blood in cases of leukæmia (*Bennett* (1852), *Virchow*). *Bizzozero* and *Salvioli* found that, several days after severe hæmorrhage, the spleen became enlarged, and its parenchyma contained numerous red nucleated hæmatoblasts.

(3) Other observers (*Kölliker and Ecker*) regard the spleen as an organ in which **coloured blood-corpuscles are destroyed**, and they consider the large protoplasmic cells containing pigment granules as a proof of this (p. 168). According to the observations of Kusnetzow, these structures are merely lymph-corpuscles, which, in virtue of their amœboid movements, have entangled coloured blood-corpuscles. [Such corpuscles exhibit similar properties when placed upon a warm stage.] Similar cells occur in extravasations of blood. The coloured blood-corpuscles within the lymph-cells gradually become disintegrated, and give rise to the production of granules of hæmatin and other derivatives of hæmoglobin. [The spleen contains so much free iron that a section of this organ, especially from a young animal, when treated with Tizzoni's fluid, *i.e.*, with potassic ferrocyanide and hydrochloric acid, gives a distinct blue colour (§ 174, 4).] Hence the spleen contains more *iron* than corresponds to the amount of blood present in it. When we consider that the spleen contains a large number of extractives derived from the decomposition of proteids, it is very probable that coloured blood-corpuscles are destroyed in the spleen. Further, the juice of the spleen contains salts similar to those that occur in the red blood-corpuscles.

The blood from the spleen is said to have undergone other changes, but the following statement must be accepted with caution :—The **blood of the splenic vein** contains more water and fibrin, its red blood corpuscles are smaller, brighter, less flattened, more resistant, and do not form rouleaux ; its hæmoglobin crystallises more easily, and there is a large proportion of O during digestion. [The serum of the blood of the splenic vein does not differ from that of the blood of the body generally.]

[The spleen has therefore very direct relations to the blood ; in it coloured blood-corpuscles undergo disintegration, it produces colourless corpuscles, and it is said to transform white corpuscles into red. The last statement, however, does not agree with the view that the red and white corpuscles are each developed from special corpuscles, and that, in fact, they are developed independently of each other (p. 13).]

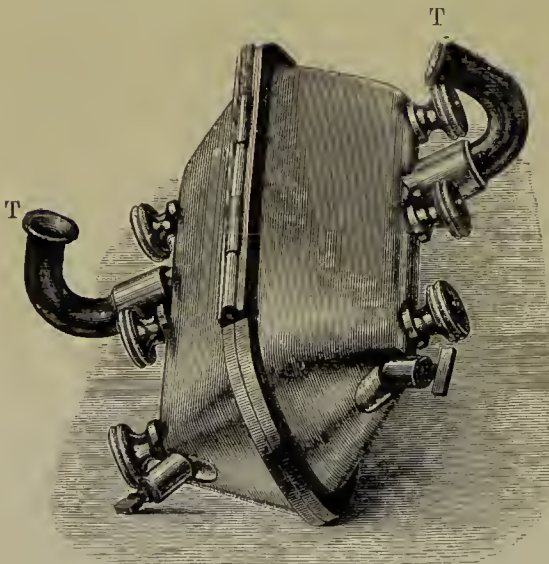


Fig. 138.

Roy's Oncometer for the spleen. T, T, tubes to be connected to the oneograph.

(4) **Contraction.**—In virtue of the plain muscular fibres in its capsule and trabeculae, the spleen undergoes variations in its volume. Stimulation of the spleen or its nerves, by cold, electricity, quinine, eucalyptus, ergot of rye, and other "**splenic reagents**" causes it to contract, whereby it becomes paler, and its surface may even appear granular. *After a meal*, the spleen increases in size, and it is usually largest about five hours after digestion has begun, *i.e.*, at a time when the digestive organs have almost finished their work and have again become less vascular. After a time it regains its original volume. For this reason the spleen was formerly regarded as an apparatus for regulating the amount of blood in the digestive organs. [The congestion of the spleen after a meal is more probably related to the formation of

new colourless corpuscles than to the destruction of red corpuscles. It may be, however, that some of the products of digestion are partially acted upon in the spleen, and undergo further change in the liver.] There is a relation between the

size of the spleen and that of the liver, for it is found that when the spleen contracts—*e.g.*, by stimulation of its nerves—the liver becomes enlarged, as if it were injected with more blood than usual (*Drosdow*).

[**Oncograph.**—Botkin, and more recently Roy, have studied various conditions which affect the size of the spleen.

Roy enclosed the spleen of a dog in a box with rigid walls (figs. 138, 139) the **oncometer** (ὄγκος, volume) and filled with oil after the manner of the plethysmograph (§§ 101, 276). Any variations in the size of the organ caused a variation in the amount of oil within the box, and these variations were recorded by means of the oncograph (§ 276). The blood-pressure was recorded at the same time. The circulation through the spleen is peculiar, and is not due to the blood-pressure within the arteries, but is carried on chiefly by a rhythmical contraction of the muscular fibres of the capsule and trabeculae. The spleen undergoes very regular rhythmical contractions (**systole**) and dilatations (**diastole**). This alternation of systole and diastole may last for hours, and the two events together occupy about one minute (fig. 140). Changes in the arterial

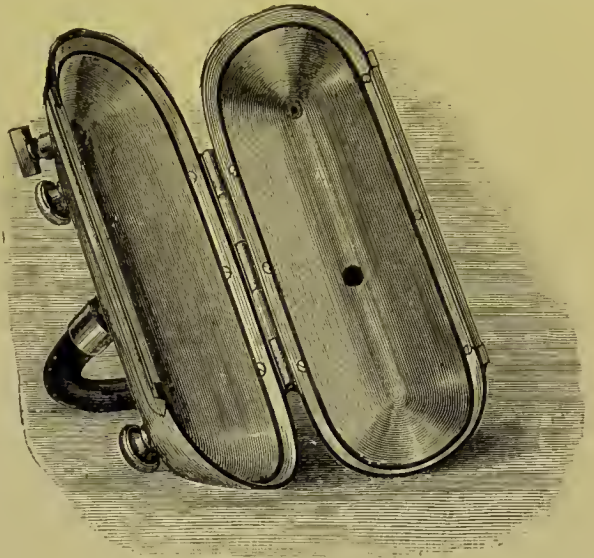


Fig. 139.

Fig. 138 shown open.

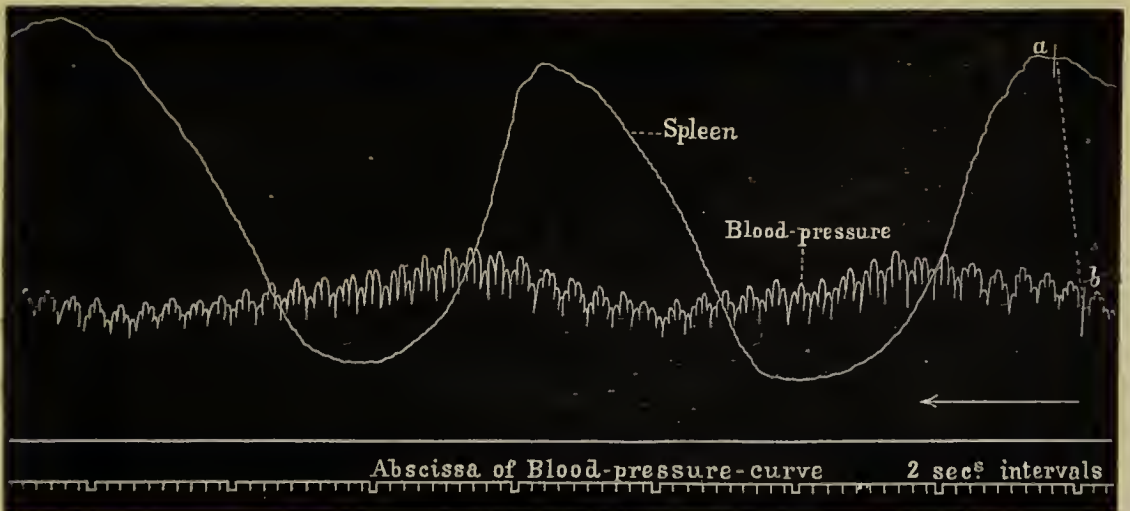


Fig. 140.

Tracing of a splenic curve, reduced one-half, taken with the oncograph. The upper line with large waves is the splenic curve, each ascent corresponds to an increase, and each descent to a diminution in the volume of the spleen. The curve beneath is a blood-pressure tracing from the carotid artery. The lowest line indicates the time, the interruptions of the marker occurring every two seconds. The vertical lines, *a* and *b*, give the relative positions of the lever-point of the oncograph, and of the point of the recording style of the kymograph respectively (*Roy*).

blood-pressure have comparatively little influence on the volume of the spleen. The rhythmical contractions, although modified, still go on after section of the

splenic nerves. This would seem to indicate that the spleen has an independent (nervous) mechanism within itself, causing its movements.]

[Influence of Nerves.]—Section of the splenic nerves is followed by an increase in the size of the spleen. The nerves have their centre in the medulla oblongata. Stimulation of the medulla oblongata, either directly or by means of asphyxiated blood, causes contraction of the spleen, hence the spleen is “small and contracted” in death from asphyxia. The fibres proceed down the cord, and leaving it in the dorsal region, enter the left splanchnic, pass through the semi-lunar ganglion, and thus reach the splenic plexus. Stimulation of the peripheral ends of these nerves causes contraction of the spleen, and so does cold applied to the spleen directly or over the region of the organ. In the last case the result is brought about reflexly. Botkin found that the application of the induced current to the skin over the spleen, in a case of leukæmia, caused well-marked contraction of the spleen in all its dimensions, and the result lasted some time. After every stimulation the number of colourless corpuscles in the blood increased, and the condition of the patient improved.]

[There is a popular notion that the spleen is influenced by the condition of the nervous system. Botkin found that depressing emotions increased its size, while exhilarating ideas diminished it. The **causes** of these changes are referable not only to changes in the amount of blood in the spleen, but also to the greater or less degree of contraction of its muscular tissue. And it would appear that, like the small arteries, the muscular tissue of the spleen is in a state of **tonic contraction**. The size of the spleen may be influenced **reflexly**. Thus, Tarchanoff found that stimulation of the *central* end of the vagus, when the splanchnics were intact, caused contraction of the spleen, while stimulation of the *central* end of the sciatic also caused contraction, but to a less degree. It is quite certain that all the phenomena are not due to the action of vaso-motor nerves on the splenic blood-vessels. There is a certain amount of independent action of the muscular fibres of the organ, and it is not improbable that the innervation of the spleen is similar to the innervation of arteries, and that it has a motor centre in the cord capable of being influenced reflexly by afferent nerves, while it also sends out efferent impulses.]

[Stimulation of (1) the central end of a sensory nerve; (2) of the peripheral ends of both splanchnics; (3) of the peripheral ends of both vagi, causes contraction of the spleen. But even after section of the splanchnics and vagi, stimulation of a sensory nerve still causes contraction, so that there must be some other channel as yet unknown (*Roy*). Bochefontaine found that electrical stimulation of certain parts of the cortex cerebri produced contraction of the spleen.] *Sensory* nerves seem to occur only in the peritoneum covering the spleen.

Pressure on the splenic vein causes enlargement of the spleen, hence increased pressure in this vein (congestion of the portal vein, cessation of hæmorrhoidal and menstrual discharges) also causes its enlargement. With regard to the action of “**splenic reagents**,” such as **quinine**, on the contraction of the spleen, Binz is of opinion that this drug retards the formation of the colourless blood-corpuscles, so that its chief function is interfered with, and the organ becomes less vascular. It is not definitely decided, however, whether it is contraction or dilatation of the spleen that alters the proportion of red and white corpuscles in the blood.

Splenic Tumours.—The increase in size of the spleen in various diseases early attracted the attention of physicians. The healthy spleen undergoes several variations in volume during the course of a day, corresponding with the varying activity of the digestive organs. In this respect the spleen resembles the arteries. In many fevers the spleen becomes greatly enlarged, probably due to paralysis of its nerves. It is greatly increased in intermittent fever or ague, and often during the course of typhus. When it becomes abnormally enlarged, and remains so after repeated attacks of ague, it is greatly hypertrophied, and constitutes “**ague cake**.” In cases of splenic leukæmia it is greatly enlarged, and at the same time there is a great increase in the number of colourless corpuscles in the blood and also a decrease of the coloured ones (§ 10).

II. The Thymus.—During foetal life this gland is largely developed, and it increases during the first two or three years of life, remaining stationary until the

tenth or fourteenth year, when it begins to atrophy and undergo fatty degeneration. [The degeneration begins at the outer part of each lobule and progresses inwards (*His*). Waldeyer finds that even in the oldest person the thymus is always represented by a mass of fat, at least as large as the thymus at birth, and always containing some adenoid tissue either in a diffuse or nodular form.]

Structure.—"It consists of an aggregation of lymph-follicles (resembling the glands of Peyer) or masses of adenoid tissue held together by a framework of connective-tissue which contains blood-vessels, lymphatics, and a few nerves (fig. 141). The **framework** of connective-tissue gives off septa which divide the gland into **lobes**, these being further subdivided by finer septa into **lobules**, the lobules being separated by fine intra-lobular lamellæ of connective-tissue into **follicles** (0.5–1.5 mm.). These follicles make up the gland-substance, and they are usually polygonal when seen in a section. Each follicle consists of a **cortical** and a **medullary** part, and the matrix or framework of both consists of a fine adenoid reticulum whose meshes are filled with lymph-corpuscles" (fig. 142, *a*). Many of these corpuscles exhibit various stages of disintegration. In the medulla are found the **concentric corpuscles of Hassal**. ["They consist of a central granular part, around which are disposed layers of flattened nucleated endothelial cells arranged concentrically. When seen in a section they resemble the 'cell-nests' of epithelioma (fig. 142, *b*). They have also been compared to similar bodies which occur in the prostate. They are most numerous when the gland undergoes its retrograde metamorphosis." Sig. Mayer finds that the thymus of the frog contains structures, with transverse markings, identical with the stripes of striped muscular fibres. The structures are identical with those called "**sarcoplasts**" by Margo and Paneth, and "**sarcolytes**" by Sig. Mayer. They also occur in large numbers in the tail of the larvæ of batrachians, when the tail is undergoing a retrograde metamorphosis.]

Simon, His, and others described a convoluted blind canal, the "**central canal**," as occurring within the gland, and on it the follicles were said to be placed. Other observers, Jendrassik and Klein, either deny its existence or regard it merely as a lymphatic or an artificial product. Numerous fine **lymphatics** penetrate into the interior of the organ, and many are distributed over its surface, but their mode of origin is unknown. [They seem to be channels through which the lymph-corpuscles are conveyed away from the gland.] Numerous **blood-vessels** are also distributed to the septa and follicles (fig. 141, *c*).

Chemical Composition.—Besides gelatin, albumin, soda-albumin, there are sugar and fat, leucin, xanthin, hypoxanthin, formic, acetic, butyric, and succinic acids. Potash and phosphoric acid are more abundant in the *ash* than soda, calcium, magnesium (? ammonium), chlorine, and sulphuric acid.

Function of the Thymus.—As long as it exists, it seems to perform the functions of a true lymph-gland. This view is supported by the fact that in reptiles and amphibians, which do not



Fig. 141.

Section of the thymus gland of a cat, with one complete lobule with a cortical part *a*, and a centre, *b*. *a*, lymphoid tissue; *c*, blood-vessels injected; *d*, connective-tissue.

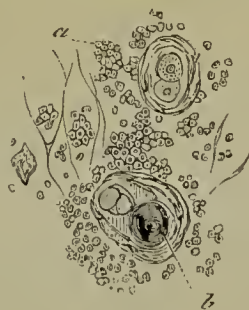


Fig. 142.

Elements of the thymus ($\times 300$). *a*, lymph-corpuscles; *b*, concentric corpuscle of Hassall.

Numerous **blood-vessels** are also

possess lymph-glands, the thymus remains as a permanently active organ. [Extirpation gave few positive results, but chemical investigation shows that the parenchyma contains a large number of products indicating considerable metabolic activity (*Friedleben*).]

[**Development of the Thymus.**—The thymus is the organ which earliest shows the structure of adenoid tissue, both in the ontogeny of individual mammals and in the phylogeny of the vertebrates. In man His maintains that it is derived from the epithelium covering the fourth, third, and part of the second branchial cleft, which becomes compressed in the angle between the head and neck. (More recent observers—Kastuchenko and others—have thrown some doubt on the correctness of His's observations; probably there are considerable differences in different classes of vertebrates, but all are now agreed that the original thymus is an epithelial organ mainly derived from the epithelium covering the gill-clefts.) The tube of epithelium—*sinus præcervicalis*—so formed grows inwards, branching dichotomously, and ramifying in the connective-tissue behind the sternum, just above the pericardium. The cells forming it grow inwards and fill up the lumen of the “gland,” and at last of the duct also. By this epithelial ingrowth the same condensation of connective-tissue is brought about as in the tonsil, and in the same way blood-vessels appear in large numbers, and leucocytes begin to wander out of the vessels, are detained in the meshes of the connective-tissue, and invade the nearly functionless epithelial gland lobules. The cells of the latter proliferate, and the older cells of the lobule are pushed to the centre, become cornified, and present very much the appearance of the cell-nests of an epithelioma, forming the so-called “concentric corpuscles of Hassall.” While the leucocytes soon eat away the majority of the epithelial cells, and break the continuity of the epithelial tubes, these cornified structures long resist their attacks, and the thymus always retains the lobular character imparted to it by its epithelial precursor. The leucocytes divide rapidly by mitosis in the connective-tissue surrounding these epithelial remains, though no true “germ-centres” are ever formed. The complete removal of the “concentric corpuscles” by the leucocytes leads to the disappearance of the latter, and the appearance of fat in the position of the thymus; but Waldeyer has recently shown that the outward form of the thymus is always preserved in this fatty mass, and that it is always possible to demonstrate microscopically in some part of it a remaining leucocyte infiltration, and wherever this is at all well marked it will be found to surround a surviving “concentric corpuscle” (*G. L. Gulland*).]

III. The Thyroid.—Structure.—The gland consists of lobes and lobules held together by connective-tissue rich in cells. Each lobule is made up of numerous completely closed sacs (0.04 to 0.1 mm. in diameter), which in the embryo and the newly-born animal are composed of a *membrana propria* lined by a single layer of nucleated cubical cells (fig. 143). The sacs contain a transparent, viscid, albuminous fluid. [Not unfrequently the sacs contain many coloured blood-corpuscles (*Baber*).] Each sac is surrounded by a plexus of capillaries which do not penetrate the *membrana propria*. There are also numerous lymphatics. At an early period the sacs dilate, their cellular lining atrophies, and their contents undergo colloid degeneration. When the gland-vesicles are greatly enlarged, “goitre” is produced.

The chemical composition of this gland has not been much investigated. In addition to the ordinary constituents, leucin, xanthin, sarkin, lactic, succinic, and volatile fatty acids have been found.

[**Excision.**—The effects differ according to the animal operated on. This gland has been excised in the human subject in cases of goitre. Reverdin pointed out that a peculiar condition results, called *cachexia stupida*, and practically the human being becomes a cretin. This operation therefore is highly questionable when performed on man. Rabbits endure the operation well, and so do the sheep, calf, and horse, none of the remarkable symptoms that occur in the dog and monkey being manifested by them. In pigeons no obvious disturbance is produced after bilateral excision of these glands, so that they do not appear to perform any important function in these animals (*R. Ewald*). Of dogs, cats, and foxes, only a very small number survive; nearly all die. It appears therefore that herbivora bear the operation and suffer fewer after-effects than carnivora (*Sanguirico and Orecchia*). The immediate effects are fibrillar contractions, which ultimately influence the gait of the animals, convulsions, anaesthesia, great diminution of sensibility, loss of flesh, redness of the ears, and intense heat of the skin (which disappear after several days), difficulty in seizing and eating food, kerato-conjunctivitis, and frequently disturbance of the rhythm of respiration with dyspnoea and spasms of the abdominal muscles (*Schiff*). The arterial blood contains about the same amount of O as venous blood. Certain parts of the peripheral nerves undergo a kind of degeneration similar to that found after nerve-stretching. There is albuminuria and fall of the blood-pressure. Death usually occurs between the third and fourth day, the animals being comatose (*Wagner*). Schiff found that if one-half of the gland was excised at once, and the other half a month afterwards, death did

not occur ; but Wagner denies this, for he asserts, that the remaining half hypertrophies, and if it be excised, death occurs with the usual symptoms. In **monkeys**, five days after the operation, there are symptoms of nervous disturbance. The animals have lost their appetite, there are fibrillar contractions of the muscles of the face, hands, and feet, but the tremors disappear on voluntary effort. The appetite returns and is increased, but notwithstanding, the animal grows thin and pale ; while the tremors increase and affect all the muscles of the body. These tremors are of *central* origin, because they disappear on dividing the nerve. Thus there is profound alteration of the motor powers. Amongst the outwardsymptomsare puffiness of the eyelids, swelling of the abdomen, increased hebetude and dyspnœa, while afterwards there is a fall of the temperature and imbecility ; the tremors disappear, there is a palor of the skin, and ultimately, after five to seven weeks, the animals die comatose. Thus there is slow onset of hebetude, terminating in imbecility. Very remarkable changes occur in the blood. There is a steady fall of the blood-pressure ; a diminution of the red blood-corpuscles, or rather profound anæmia ; leucocythæmia, the colourless corpuscles being increased to the ratio of four to fourteen ; and lastly **mucin** is present in the blood, although normally it is not so. The salivary glands are hypertrophied, owing to the presence of mucin, which is found even in the parotid, although this is normally a serous gland (§ 141). The swelling of the abdomen is due to hypertrophy of the great omentum. Mucin is found in the peritoneal fluid, and the spleen is also enlarged. Thus these symptoms present many features in common with those of **myxœdema** as described by Ord (*v. Horsley*).]

[**Stages**.—Horsley distinguishes three stages. In the first or **neurotic** stage, the animals exhibit constant tremors, 8 per second, and young animals do not appear to survive this stage. In the second or **mucinoid** stage, mucin is deposited in the tissues and blood ; this change, however, is only seen to perfection in monkeys. If these animals be kept at a high artificial temperature, their life is considerably prolonged. In the third, **atrophic** or **marasmic** period, the animals die of marasmus, while they lose their excess of mucin. **Age** seems to exert an important influence in thyroidectomy ; young dogs survive but a short time, while old dogs merely exhibit symptoms of indolence and incapacity ; and, as a matter of fact, the activity of the gland seems to be most active when tissue-metabolism is most active.]

The following table, after Horsley, indicates the symptoms that follow loss of the function of the thyroid gland.

Stages.	Duration.	Symptoms.	Remarks.
I. Neurotic.	1 to 2 weeks in dogs ; 1 to 3 weeks in monkeys.	Tremors, rigidity, dyspnœa.	Young dogs and monkeys alike die in this stage.
II. Mucinoid.	$\frac{1}{2}$ to 1 week in dogs ; 3 to 7 weeks in monkeys.	Commencing hebetude and mucinoid degeneration of the connective-tissues.	Dogs survive only to the beginning of this stage ; monkeys die at the end, if not treated.
III. Atrophic.	5 to 8 weeks in monkeys.	Complete imbecility and atrophy of all tissues, especially muscles.	Monkeys survive according to the temperature of the air-bath.]

Functions.—The functions of the thyroid gland are very obscure. Perhaps it may be an apparatus for regulating the blood-supply to the head (?). It becomes enlarged in **Basedow's disease**, in which there is great palpitation, as well as protrusion of the eyeballs or exophthalmos, which seem to depend upon a simultaneous stimulation of the accelerating nerve of the heart, and the sympathetic fibres of the smooth muscles in the orbital cavity and the eyelids, as well



Fig. 143.

Section of the thyroid gland. *a*, closed vesicles ; *b*, distended by colloid masses and lined by low columnar epithelium ; *c*, inter-vesicular connective tissue.

as of the inhibitory fibres of the vessels of the thyroid. In many localities it is common to find swelling of the thyroid constituting **goitre**, which is sometimes, but far from invariably, associated with idiocy and cretinism. [Horsley finds that its removal is the essential cause of myxœdema and cretinism. He regards it (1) as a **blood-forming gland**, so that it has a hæmopoietic function, but Gibson finds no grounds for supporting this view. During the anæmia resulting from its removal, the blood of the thyroid vein contains 7 per cent. more red blood-corpuscles than the corresponding artery (*Horsley*). (2) It seems to regulate the formation of **mucin** in the body. After its removal the normal metabolism is no longer maintained, and there is a corresponding increasingly defective condition of nutrition.]

According to Rogowitsch, the function of the thyroid is to neutralise a substance produced in the body, which, if it accumulated, would act as a poison on the central nervous system.

[**Transplantation of the Thyroid.**—Part of the thyroid of animals has been transplanted to the abdominal cavity and under the skin, but apparently, when so transplanted, fails to exercise any beneficial influence in cases of myxœdema.]

In the Tunicata, this gland, represented by a groove, secretes a digestive fluid. In vertebrates it is an organ which has undergone a retrograde change (*Gegenbaur*).

IV. The Suprarenal Capsules.—Structure.—These organs are invested by a thin **capsule** which sends processes into the substance of the organ. They consist of an outer (broad) or **cortical** layer and an inner (narrow) or **medullary** layer (fig. 144). The former is yellowish in colour, firm and striated, while the latter is softer and deeper in tint. In the outermost zone of the **cortex** (fig. 145), the trabeculæ form polygonal meshes, which contain the cells of the gland-substance; in the broader middle zone the meshes are elongated, and the cells filling them are arranged in columns radiating outwards. Here the cells are transparent and nucleated, often containing oil-globules; in the innermost narrow zone the polygonal arrangement prevails, and the cells often contain yellowish-brown pigment. [Immediately under the capsule the cells are arranged in rounded groups—**zona glomerulosa**; next to this the cells are arranged in columns, forming the widest zone or **zona fasciculata**, while next the medulla is the **zona reticularis** (fig. 145).] In the **medulla** the stroma forms a reticulum containing groups of cells of very irregular shape. Numerous **blood-vessels** occur in the gland, especially in the cortex. [The **nerves** are extremely numerous, and are derived from the renal and solar plexuses. Many of the fibres are medullated. After they enter the gland, numerous ganglionic cells occur in the plexuses which they form. Indeed, some observers regard the cells of the medulla as nervous. Undoubtedly, numerous *multipolar nerve-cells* exist within the gland.]

Chemical Composition.—The suprarenals contain the constituents of connective- and nerve-tissue; also leucin, hypoxanthin, benzoic, hippuric, and taurocholic acids, taurin, inosit, fats, and a body which becomes pigmented by oxidation. Amongst inorganic substances potash and phosphoric acid are most abundant.

[**Poisonous Extract.**—Foa and Pellacani showed that a watery extract of the supra-renal capsule is poisonous to dogs, rabbits, and frogs. Marino-zucco has shown that the toxic base is **neurin**.]

The function of the suprarenal bodies is very obscure. It is noticeable, however, that in **Addison's disease**, or '**bronzed skin**,' which is perhaps primarily a nervous affection, these glands have frequently, but not invariably, been found to be diseased. Owing to the injury to adjacent abdominal organs, **extirpation** of these organs is often, although not always, fatal; in dogs pigmented patches have been found in the skin near the mouth. [Tizzoni has found that many months after the excision of one or both supra-renals in dogs and rabbits, there is a profound alteration of the central nervous system. There is degeneration of the medullated nerve-fibres of certain parts of the cortex and white matter, and also of the grey and white matter of the cord. In the latter Goll's column is specially affected, but the degenerated fibres are by no means confined to it.] Brown-Séquard thinks they may be concerned in preventing the over-production of pigment in the blood.

[**Spectrum.**—MacMunn finds that the medulla of the suprarenal bodies (in man, cat, dog, guinea-pig, rat, &c.) gives the spectrum of hæmochromogen (§ 18), while the cortex shows that of what he calls **histohæmatin**, the latter being a group of respiratory pigments. He finds that hæmochromogen is only found in excretory organs (the bile, the liver), hence he regards the medulla as **excretory**, so that part of the function of the adrenals may be "to metamorphose effete hæmoglobin or hæmatin into hæmochromogen," and when they are diseased, the effete pigment is not removed, hence the pigmentation of the skin and mucous membranes.

Taurocholic acid has been found in the medulla by Vulpian, and pyro-catechin by Krukenberg. MacMunn believes that "they have a large share in the downward metamorphosis of colouring matter."]

V. Hypophysis Cerebri—Coccygeal and Carotid Glands.—The **hypophysis cerebri**, or **pituitary body**, consists of an anterior lower or larger lobe, partly embracing the posterior lower or smaller lobe. These two lobes are distinct in their structure and development. The *posterior* lobe is a part of the brain, and belongs to the infundibulum. The nervous elements are displaced by the ingrowth of connective-tissue and blood-vessels. The *anterior* portion represents an inflected and much altered portion of ectoderm, from which it is developed. It contains gland-like structures, with connective-tissue, lymphatics, and blood-vessels, the whole being surrounded by a capsule. According to Ecker and Mihalkowicz, it resembles the suprarenal capsule in its structure, while, according to other observers, in some animals it is more like the thyroid. Its functions are entirely unknown.

[**Excision.**—Horsley has removed this gland twice successfully in dogs, which lived from five to six months. No nervous or other symptoms were noticed, but when the cortex of the brain was exposed and stimulated, a great increase in the excitability of the motor regions was induced, even slight stimulation being followed by violent tetanus and prolonged epilepsy.]

Coccygeal and Carotid Glands.—The former, which lies on the tip of the coccyx, is composed to a large extent of plexuses of small, more or less cavernous arteries, supported and enclosed



Cortex. Medulla. Vein.

Fig. 144.

Part of the supra-renal capsule of a child $\times 15$.

by septa and a capsule of connective-tissue (*Luschka*). Between these lie polyhedral granular cells arranged in networks. The carotid gland has a similar structure (p. 90). Their functions are quite unknown. Perhaps both organs may be regarded as the remains of embryonal blood-vessels (*Arnold*).

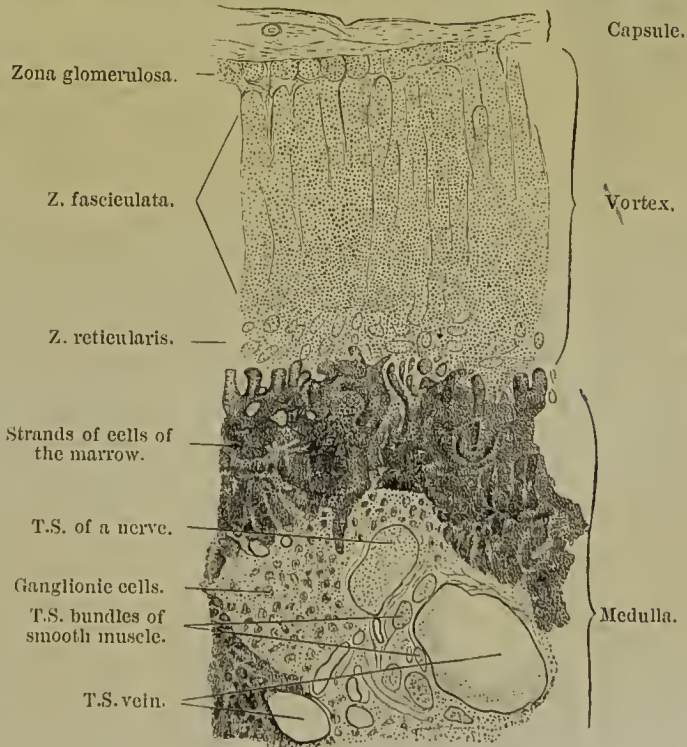


Fig. 145.

T.S., human supra-renal capsule $\times 50$.

104. COMPARATIVE. —

The heart in fishes (fig. 146, I.), as well as in the larvæ of amphibians with gills, is a **simple venous heart**, consisting of an auricle and a ventricle. The ventricle propels the blood to the gills, where it is oxygenated (arterialised); thence it passes into the aorta to be distributed to all parts of the body, and returns through the capillaries of the body and the veins to the heart. The **amphibians** (frogs) have **two auricles** and **one ventricle** (Frog, II.). From the latter there proceeds *one* vessel which gives off the pulmonary arteries, and as the aorta supplies the rest of the body with blood, the veins of

the systemic circulation carry their blood to the right auricle, those of the lung into the left auricle. In fishes and amphibians there is a dilatation at the commencement of the aorta, the

bulbus arteriosus, which is partly provided with strong muscles. The reptiles (III.) possess two separate auricles, and two imperfectly separated ventricles. The aorta and pulmonary artery arise separately from the latter two chambers. The venous blood of the systemic and pulmonary circulations flows separately into the right and left auricles, and the two streams are mixed in the ventricle. In some reptiles the opening in the ventricular septum seems capable of being closed. The complete separation of the ventricle into two is seen in fig. IV., in the tortoise. The lower vertebrates have valves at the orifices of the venæ cavæ, which are rudimentary in birds and some mammals. All birds and mammals have two completely separate auricles and two separate ventricles. In the halibore the apex of the ventricles is deeply cleft. Some animals have accessory hearts, *e.g.*, the eel in its caudal vein. They are very probably lymph-hearts (*Robin*). The veins of the wing of the bat pulsate (*Schiff*). The lowest vertebrate, *amphioxus*, has no heart, but only a rhythmically-pulsating vessel.

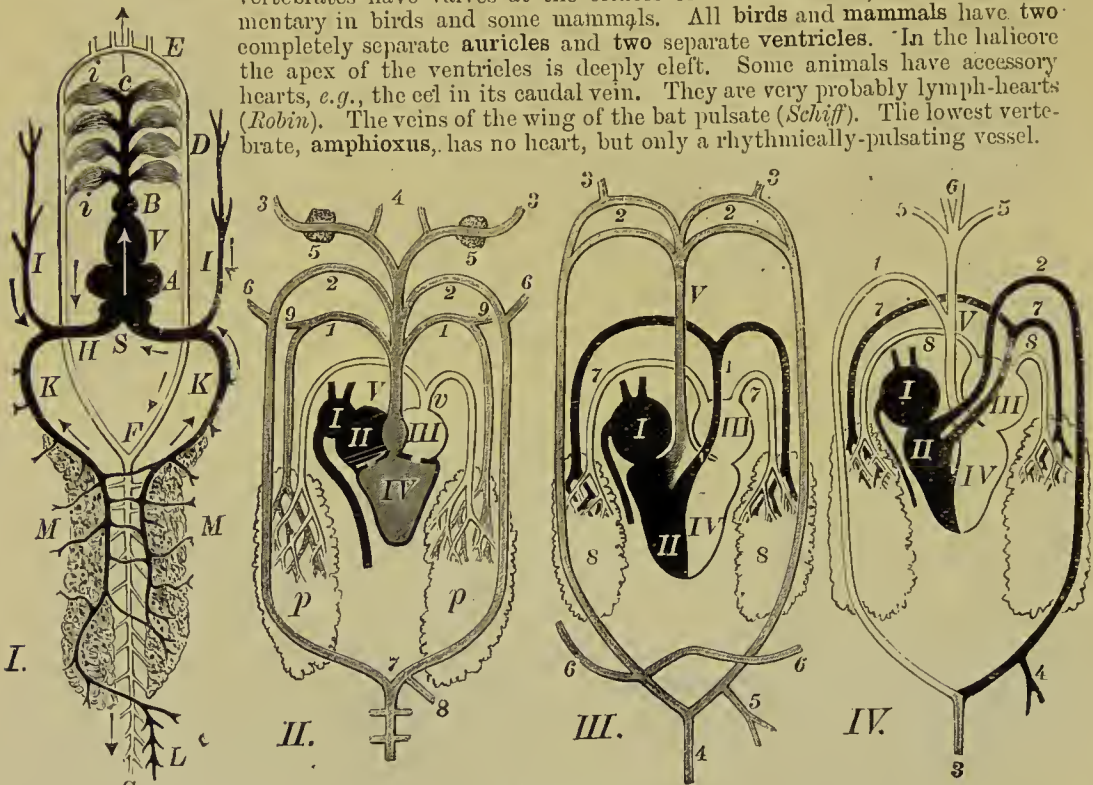


Fig. 146.

Schemata of the circulation. I. *Fish*.—A, auricle; S, sinus venosus; V, ventricle; B, bulbus aortæ; c, branchial arteries; i, branchial vessels; Vv, branchial veins; E, circulus cephalicus aortæ; F, common aorta; G, caudal artery; H, duct of Cuvier; I, anterior, and K, posterior cardinal veins; L, caudal vein; M, M, kidneys. II. *Frog*.—I, sinus venosus; II, and III, right and left auricles; IV, ventricle; V, aorta with the bulb; 1, pulmonary arteries; 2, arch of the aorta; 3, carotid; 4, lingual; 5, carotid gland, and 6, axillary arteries; 7, common aorta; 8, celiac artery; 9, cutaneous artery; Vv, pulmonary veins; p, p, lungs. III. *Saurians*.—I, right auricle, with the venæ cavæ; II, right ventricle; III, left auricle; IV, left ventricle; V, anterior common aorta; 1, pulmonary artery, 2, arch of the aorta; 3, carotid artery; 4, posterior common aorta; 5, celiac, and 6, subelavian, arteries; 7, pulmonary veins; 8, lungs. IV. *Tortoise*.—I, right auricle with the venæ cavæ; II, right, and IV, left ventricles; III, left auricle; 1 and 2, right and left aortæ; 3, posterior common aorta; 4, celiac, 5, subelavian, 6, carotid, and 7, pulmonary arteries; 8, pulmonary veins.

Amongst blood-glands, the thymus and spleen occur throughout the vertebrata, the latter being absent only in *amphioxus* and a few fishes.

Amongst *invertebrata* a closed vascular system, with pulsatile movement, occurs here and there, *e.g.*, amongst *echinodermata* (star-fishes, sea-urchins, holothurians) and the higher worms. The *insects* have a pulsating "dorsal vessel" as the central organ of the circulation, which is a contractile tube provided with valves and dilated by muscular action; the blood being propelled rhythmically in one direction into the spaces which lie amongst the tissues and organs, so that these animals do not possess a closed vascular system. The *mollusca* have a heart with a lacunar vascular system. The *cephalopods* (cuttle-fish) have three hearts—a simple arterial heart, and two venous simple gill-hearts, each placed at the base of the gills. The vessels form a completely closed circuit. The lowest animals have either a pulsatile vesicle, which propels the colourless juice into the tissues (*infusoria*), or the vascular apparatus may be entirely absent.

105. HISTORICAL RETROSPECT.—The ancients held various theories regarding the movement of the blood, but they knew nothing of its *circulation*. According to Aristotle (384 B.C.), the heart, the acropolis of the body, prepared in its cavities the blood, which streamed through the arteries as a nutrient fluid to all parts of the body, but never returned to the heart. With Herophilus and Erasistratus (300 B.C.), the celebrated physicians of the Alexandrian school, originated the erroneous view that the arteries contain air, which was supplied to them by the respiration (hence the name *artery*). They were led to adopt this view from the empty condition of the arteries after death. By experiments upon animals, Galen disproved this view (131–201 A.D.)—"Whenever I injured an artery," he says, "blood always flowed from the wounded vessel. On tying part of an artery between two ligatures, the part of the artery so included is always filled with blood."

Still, the idea of a single *centrifugal* movement of the blood was retained, and it was assumed that the right and left sides of the heart communicated directly by means of openings in the septum of the heart, until Vesalius showed that there are no openings in the septum. Michael Servetus (a Spanish monk, burned at Geneva, at Calvin's instigation, in 1553) discovered the pulmonary circulation. Cesalpinus confirmed this observation, and named it "*Circulatio*." Fabricius ab Aquapendente (Padua, 1574) investigated the valves in the veins more carefully (although they were known in the 5th century to Theodoretus, Bishop in Syria), and he was acquainted with the *centripetal* movement of the blood in the veins. Up to this time it was imagined that the veins carried blood from the centre to the periphery, although Vesalius was acquainted with the centripetal direction of the blood-stream in the large venous trunks. At length William Harvey, who was a pupil of Fabricius (1604), demonstrated the complete circulation (1616–1619), and published his great discovery in 1628. [For the history of the discovery of the circulation of the blood, see the works of Willis on "*W. Harvey*," "*Servetus and Calvin*," those of Kirchner, and the various Harveian orations.]

According to Hippocrates, the heart is the origin of all the vessels; he was acquainted with the large vessels arising from the heart, the valves, the chordæ tendineæ, the auricles, and the closure of the semi-lunar valves. Aristotle was the first to apply the terms *aorta* and *venæ cavae*; the school of Erasistratus used the term *carotid*, and indicated the functions of the venous valves. In Cicero a distinction is drawn between arteries and veins. Celsus mentions that if a vein be struck below the spot where a ligature has been applied to a limb, it bleeds, while Aretæus (50 A.D.) knew that arterial blood was bright, and venous blood dark. Pliny († 79 A.D.) described the pulsating fontanelle in the child. Galen (131–203 A.D.) was acquainted with the existence of a bone in the septum of the heart of large animals (ox, deer, elephant). He also surmised that the veins communicated with the arteries by fine tubes. The demonstration of the *capillaries*, however, was only possible by the use of the *microscope*, and employing this instrument, Malpighi (1661) was the first to demonstrate the capillary circulation. Leuwenhoek (1674) described the capillary circulation more carefully, as it may be seen in the web of the frog's foot and other transparent membranes. Blanehard (1676) proved the existence of capillary passages by means of injections. William Cooper (1697) proved that the same condition exists in warm-blooded animals, and Ruyseh made similar injections. Stenson (born 1638) established the muscular nature of the heart, although the Hippocratic and Alexandrian schools had already surmised the fact. Cole proved that the sectional area of the blood-stream became wider towards the capillaries (1681). Joh. Alfons Borelli (1608–1679) was the first to estimate the amount of work done by the heart.

Physiology of Respiration.

THE object of respiration is twofold, viz., to **supply the oxygen** necessary for the oxidation processes that go on in the body, as well as to **remove the carbon dioxide** formed within the body. [Tissue-life implies the continuous and constant supply of oxygen, and hence in mammals and the higher vertebrates the lungs are relatively very large, and yield a free supply of oxygen.] The most important organs for this purpose are the **lungs**. There is an **outer** and an **inner respiration**—the former embraces the exchange of gases between the external air and the blood-gases of the respiratory organs (lungs and skin)—the latter, the exchange of gases between the blood in the capillaries of the systemic circulation and the tissues of the body.

[The pulmonary apparatus consists of (1) an immense number of small sacs—the **air-vesicles**—filled with air, and covered externally by a very dense plexus of capillaries; (2) the **air-passages**—the nose, pharynx, larynx, trachea, and bronchi communicating with (1); (3) the **thorax** with its muscles, acting like a pair of bellows, and moving the air within the lungs.]

106. STRUCTURE OF THE AIR-PASSAGES AND LUNGS.—The lungs are compound tubular glands, which separate CO_2 from the blood. Each lung is provided with an excretory duct (bronchus) which joins the common respiratory passage of both lungs—the trachea.

Trachea.—The trachea and extra-pulmonary bronchi are similar in structure. The basis of the trachea consists of 16–20 C-shaped incomplete cartilaginous hoops placed over each other. These rings consist of hyaline cartilage, and are united to each other by means of tough fibrous tissue containing much elastic tissue, the latter being arranged chiefly in a longitudinal direction. The **function of the cartilages** is to keep the tube open under varying conditions of pressure. Pieces of cartilage having a similar function occur in the bronchi and their branches, but they are absent from the bronchioles, which are less than 1 mm. in diameter. In the smaller bronchi, the cartilages are fewer and scattered more irregularly. [In a transverse section of a large **intra-pulmonary bronchus**, two, three, or more pieces of cartilage, each invested by its perichondrium, may be found.] At the points where the bronchi subdivide, the cartilages assume the form of irregular plates embedded in the bronchial wall.

An **external fibrous layer** of connective tissue and elastic fibres covers the trachea and the extra-pulmonary bronchi externally. Towards the œsophagus, the elastic elements are more numerous, and there are also a few bundles of plain muscular fibres arranged longitudinally. Within this layer there are bundles of *non-striped muscular fibres* which pass transversely between the cartilages behind, and also in the intervals between the cartilages. [These pale reddish fibres con-

stitute the **trachealis muscle**, and are attached to the inner surfaces of the cartilages at a little distance from their free ends. The arrangement varies in different animals—thus, in the cat, dog, rabbit, and rat the muscular fibres are attached to the *external* surfaces of the cartilages, while in the pig, sheep, and ox they are attached to their *internal* surfaces (*Stirling*).] Some muscular fibres are arranged longitudinally external to the transverse fibres. The **function** of these muscular fibres is to prevent too great distention when there is great pressure within the air-passages.

The **mucous membrane of the trachea** consists of a basis of very fine connective-tissue, containing much adenoid tissue with numerous lymph-corpuseles. Numerous elastic fibres are arranged chiefly in a longitudinal direction under the basement membrane. They are also abundant in the deep layers of the posterior part of the membrane opposite the intervals between the cartilages. A small quantity of loose **sub-mucous** connective tissue containing the large blood-vessels, glands, and lymphatics unites the mucous membrane to the perichondrium of the cartilages. The **epithelium** consists of a layer of columnar ciliated cells with several layers of immature cells under them. [The superficial layer of cells is columnar and **ciliated** (fig. 147, *b*), while those lying under them present a variety of forms, and below all is a layer of somewhat flattened squames, *c*, resting on the basement membrane, *d*. These squames constitute a layer quite distinct from the basement membrane, and they form the layer described as **Débove's membrane**. They are active germinating cells, and play a most important part in connection with the regeneration of the epithelium, after the superficial layers have been shed, in such conditions as bronchitis. Not unfrequently a little viscid mucus (*a*) lies on the free ends of the cilia. In the intermediate layer, the cells are more or less pyriform or battledore-shaped, with their long tapering process inserted amongst the deeper layers of cells. According to Drasch, this long process is attached to one of these cells and is an outgrowth from it, the whole constituting a "foot-cell."]

Under the epithelium is the homogeneous **basement membrane**, through which fine canals pass, connecting the cement of the epithelium with spaces in the mucosa. [This membrane is well marked in the human trachea, where it plays an important part in many pathological conditions, *e.g.*, bronchitis. It is stained bright red with

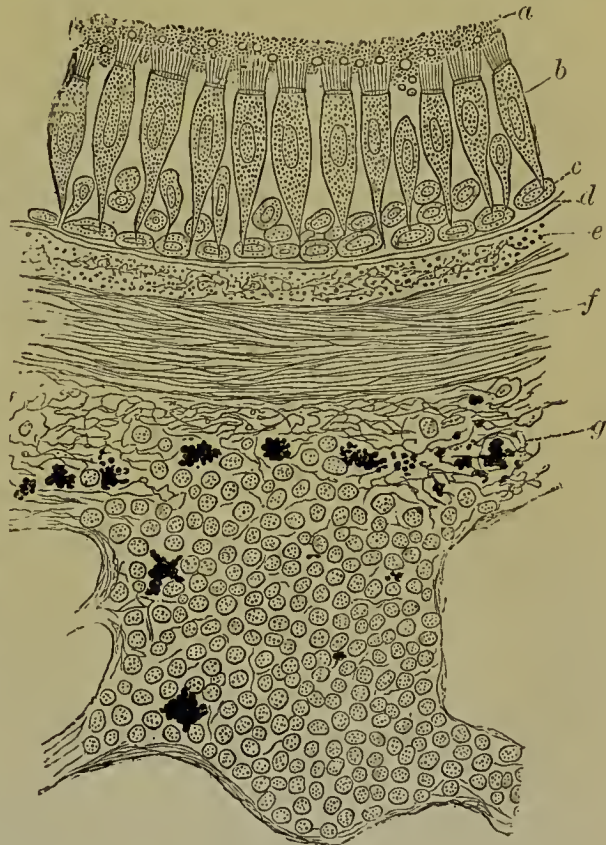


Fig. 147.

Transverse section of part of a human bronchus ($\times 450$). *a*, precipitated mucus; *b*, ciliated columnar epithelium; *c*, deep germinal layer of cells (Débove's membrane); *d*, elastic basement membrane; *e*, elastic fibres divided transversely (inner fibrous layer); *f*, bronchial muscle; *g*, outer fibrous layer with leucocytes and pigment granules (black) below mass of adenoid tissue.

microcarmine.] The cilia act so as to carry any secretion towards the larynx. Goblet cells exist between the ciliated columnar cells. Numerous small compound tubular **mucous glands** occur in the mucous membrane, chiefly between the cartilages. Their ducts open on the surface by means of a slightly funnel-shaped aperture, into which the ciliated epithelium is prolonged for a short distance. [The acini of some of these glands lie outside the trachealis muscle. The acini are lined by cubical or columnar secretory epithelium. In some animals (dog) these cells are clear, and present the usual characters of a mucus-secreting gland; in man, some of the cells may be clear, and others "granular," but the appearance of the cells depends upon the physiological state of activity.] These glands secrete the mucus, which entangles particles inspired with the air, and is carried towards the larynx by ciliary action. [Numerous **lymphatics** exist in the mucous and sub-mucous coat, and not unfrequently small aggregations of adenoid tissue occur (especially in the cat) in the mucous coat, usually around the ducts of the glands. They are comparable to the solitary follicles of the alimentary tract. The **blood-vessels** are not so numerous as in some other mucous membranes. [A plexus of **nerves** containing numerous ganglionic cells at the nodes exists on the posterior surface of the trachealis muscle. The fibres are derived from the vagus, recurrent laryngeal, and sympathetic (*C. Frankenhauser, W. Stirling, Kandarazi*).]

[The **mucous membrane of the trachea and extra-pulmonary bronchi**, therefore, consists of the following layers from within outwards:—

- (1) Stratified columnar ciliated epithelium.
- (2) A layer of flattened cells (Débove's membrane).
- (3) A clear homogeneous basement membrane.
- (4) A basis of areolar tissue, with adenoid tissue and blood-vessels, and outside this a layer of longitudinal elastic fibres.

Outside this, again, is the **sub-mucous coat**, consisting of loose areolar tissue, with the larger vessels, lymphatics, nerves, and mucous glands.]

The **Bronchi**.—In structure the **extra-pulmonary bronchi** resemble the trachea. As they pass into the lung they divide very frequently, and the branches do not anastomose. In the **intra-pulmonary bronchi** the subdivisions become finer and finer, the finest branches being called **terminal bronchi**, or **bronchioles**, which open separately into clusters of air-vesicles.]

[**Eparterial and Hyparterial Bronchi**.—As the bronchi proceed, one main trunk passes into the lung, running towards its base, and from it are given off branches dorsally and ventrally, and these branches again subdivide. In man one main branch comes off from the right bronchus and proceeds to the upper right lobe, *above* the place where the pulmonary artery crosses the bronchus. Such branches are called *eparterial*, and they are more numerous in birds. In man, all the branches, both on the right and left side, come off below the point where the pulmonary artery crosses the bronchus, and are called *hyparterial bronchi* (*C. Aeby*).]

In the middle-sized **intra-pulmonary bronchi** the usual characters of the mucous membrane are retained, only it is thinner; the cartilages assume the form of irregular plates situated in the outer wall of the bronchus; while the muscular fibres are disposed in a complete circle, constituting the **bronchial muscle** (fig. 147, *f*). When this muscle is contracted, or when the bronchus as a whole is contracted, the mucous membrane is thrown into longitudinal folds, and opposite these folds the elastic fibres form large elevations. This muscle is particularly well developed in the smaller microscopic bronchi. Numerous elastic fibres, *e*, disposed longitudinally, exist under the basement membrane, *d*. They are continuous with those of the trachea, and are prolonged onwards into the lung. The mucous membrane of the larger **intra-pulmonary bronchi** consists of the following layers from within outwards:—

- (1) Stratified columnar ciliated epithelium (fig. 147, *b*).
- (2) Débove's membrane (fig. 147, *c*).
- (3) Transparent homogeneous basement membrane (fig. 147, *d*).
- (4) Areolar tissue with longitudinal elastic fibres (fig. 147, *e*).
- (5) A continuous layer of non-stripped muscular fibres disposed circularly (*bronchial muscle*, fig. 147, *f*).

Outside this is the **sub-mucous coat**, consisting of areolar tissue mixed with much adenoid tissue (fig. 147, *g*), sometimes arranged in the form of cords, the **lymph-follicular cords**. It also contains the acini of the numerous **mucous glands**, blood-vessels, and lymphatics. The ducts of the glands perforate the muscular layer, and open on the free surface of the mucous membrane. The sub-mucous coat is connected by areolar tissue with the perichondrium of the **cartilages**. Outside the cartilages are the **nerves** and **nerve-ganglia** accompanying the bronchial vessels. The branches of the pulmonary artery and of the pulmonary vein usually lie on opposite sides of the bronchus, while there are several branches of the bronchial arteries and veins. **Fat cells** also occur in the peri-bronchial tissue.]

In the **small bronchi** the cartilages and glands disappear, but the circular muscular fibres are well developed. They are lined by lower columnar ciliated epithelium, containing goblet-cells.

[The bronchi when traced into the lung divide more or less dichotomously, and run between the lobules, constituting **inter-lobular bronchi**, and accompanied by branches of the pulmonary artery and vein. The branches become smaller and smaller until they end finally in **terminal bronchi** (.5 to 1 mm.) in diameter. These terminal bronchi or **lobular bronchi** open into the apex of a lobule. As they pass into the lobule they give off, usually at nearly a right angle, several branches—the **intra-lobular bronchi**—or **bronchioles**, sometimes spoken of as **alveolar passages**. These alveolar passages are beset on all sides by air-cells.

Each bronchiole opens into one or two wider passages, having the shape of an inverted cone, called an **infundibulum** (fig. 149, I), with delicate walls, and beset with **air-vesicles**, **air-cells** or **alveoli** (fig. 149). The cup-shaped air-vesicles open into the infundibulum, but do not communicate with each other. The infundibula are much wider than the bronchioles and also than the alveoli. Each terminal bronchiole with its infundibula and air-vesicles constitutes an **acinus** or **lobule**, and all the lobulets connected with a terminal bronchus make up a single lobule. The **lobules** are arranged with their bases externally, and are separated from each other by connective tissue—**inter-lobular septa** (fig. 149, IS)—so that in a partially pigmented lung, on examining its pleural surface with the naked eye, one can easily make out its lobules, consisting of a series of polygonal areas mapped out by black lines. In a young animal, *e.g.*, calf, they are easily separated from each other after removal of the pleura. The inter-lobular septa are continuous on the one hand with the sub-pleural connective tissue and on the other with the peri-bronchial connective tissue.]



Fig. 148.

Termination of a bronchiole and of a pulmonary arteriole prepared by corrosion and magnified by a hand lens. A, bronchiole; B, branch of pulmonary artery.

[There is an **alteration in the structure of the bronchi**, as we proceed from the larger to the smaller tubes. The cartilages and glands are the first structures to disappear. The circular bronchial muscle is well developed in the smaller bronchi and bronchioles, and exists as a continuous thin layer over the alveolar passages, but it is not continued over and between the air-cells. Elastic fibres, continuous, on the one hand, with those in the smaller bronchi, and, on the other,

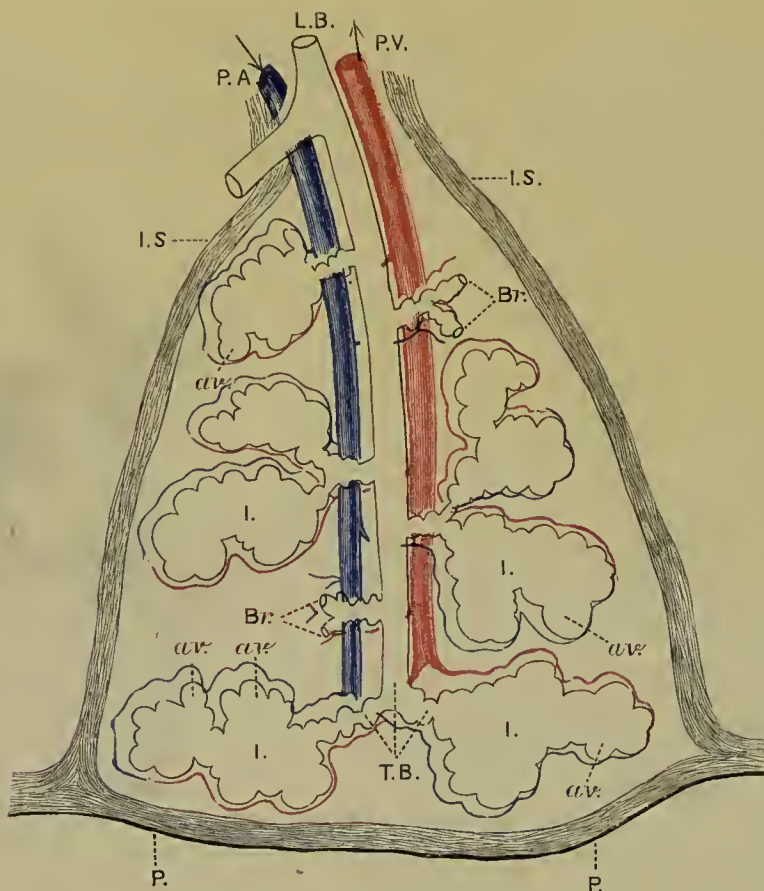


Fig. 149.

Scheme of a lung lobule. PA, and PV, pulmonary artery and vein; TB, terminal bronchus; Br., bronchiole; I, infundibulum; av, air-vesicles; IS, inter-lobular septum; PP, pleura; LB, lobular bronchus.

with those in the walls of the air-cells, lie outside the muscular fibres in the bronchioles and infundibula. In the respiratory bronchioles, the ciliated epithelium is reduced to a single layer, and is mixed with the squamous form of epithelium, while where the alveolar passages open into the air-cells or alveoli, the epithelium is non-ciliated, low, and polyhedral.]

Alveoli or Air-Cells.—The form of the air-cells, which are $25\ \mu$ ($\frac{1}{100}$ inch) in diameter, may be more or less spherical, polygonal, or cup-shaped. They are disposed around and in communication with the alveolar passages. Their form is determined by the existence of a nearly structureless membrane, composed of slightly fibrillated connective-tissue containing a few corpuscles. This is surrounded by numerous fine elastic fibres, which give to the pulmonary parenchyma its well-marked elastic characters (fig. 153, *e*, *e*). These fibres often bifurcate, and are arranged with reference to the alveolar wall. They are very resistant, and in some

cases of lung disease may be recognised in the sputum. A few non-striped muscular fibres exist in the delicate connective tissue between adjoining air-vesicles. These muscular fibres sometimes become greatly developed in certain diseases (*Arnold, W. Stirling*). The air-cells are lined by two kinds of cells—(1) large, transparent, clear polygonal non-nucleated **squames** or placoids ($22-45\ \mu$) lying over and between the capillaries in the alveolar wall (fig. 151, *a*); (2) small irregular “**granular**” nucleated cells ($7-15\ \mu$) arranged singly or in groups (two or three) in the interstices between the capillaries. They are well seen in a cat’s lung (fig. 151, *d*). When acted on with nitrate of silver the cement-substance bounding the clear cells is stained, but the small cells become of a uniform brown granular appearance, so that they are readily recognised. Small markings (? holes) or “**pseudo-stomata**” exist in the cement-substance, and are most obvious in distended alveoli. They open into the lymph-canalicular system of the alveolar wall (*Klein*), and through them the lymph-corpuscles, which are always to be found on the surface of the air-vesicles, migrate, and carry with them into the lymphatics particles of carbon derived from the air. In the alveolar walls is a very dense plexus of fine **capillaries** (fig. 153, *c*), which lie more towards the cavity of the air-vesicle, being covered only by the epithelial lining of the air-cells. Between two adjacent alveoli there is only a single layer of capillaries (man), and on the boundary line between two air-cells the course of the capillaries is twisted, thus projecting sometimes into the one alveolus, sometimes into the other (fig. 152).

[In the lung of the **newt**, which is simply an oval sac with elastic and contractile walls, supplied by an artery and a vein, the capillary network lies immediately under the epithelium. The meshes themselves are narrow, although the capillaries corresponding to the large size of the blood-corpuscles are fairly wide. The epithelium consists of a single layer of thin cells peculiarly modified. The nucleated bodies of three or more cells have an appreciable thickness and lie in the extra-vascular meshes or islands, and from each cell there stretches an excessively thin wing-shaped expansion over the surface of the capillary, to meet a similar expansion from another cell lying in an adjacent mesh or island. Thus the blood in the capillary is separated from the air in the lung only by the thin capillary wall and the excessively thin wing-like expansions of the smaller “respiratory epithelium.” The newt’s lung represents a very simple type of lung. In the **frog** the lung begins to be more complex. The infundibulum of the mammalian lung practically repeats the condition obtaining in the newt’s lung.]

[The **number of alveoli** is stated to be about 725 millions, a result obtained by measuring the size of the air-vesicles and ascertaining the amount of air in the lung, after an ordinary inspiration, determining how much of this air is in the air-vesicles and bronchi respectively. The superficial area of the air-vesicles is about 90 square metres, or 100 times greater than the surface of the body ($\cdot 8$ to $\cdot 9$ sq. metre).]

The **Blood-vessels** of the lung belong to two different systems:—(A) **Pulmonary vessels** (lesser circulation). The branches of the **pulmonary artery** accompany the bronchi and are closely applied to them. [As they proceed they branch, but

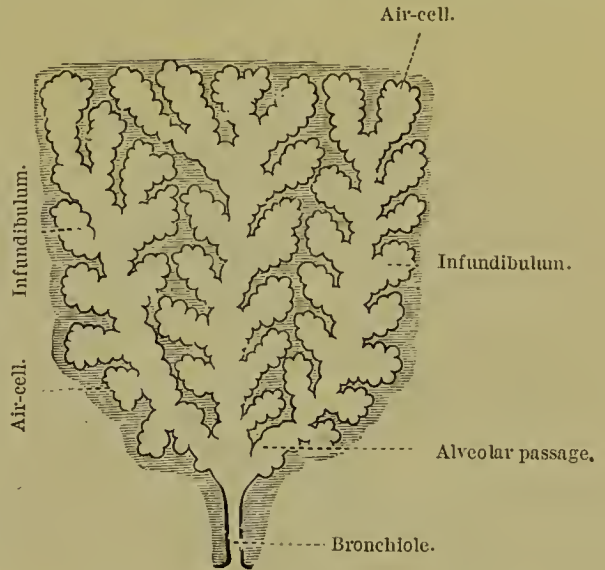


Fig. 150.

Scheme of a bronchiole terminating in alveolar passages, those leading into infundibula beset with air-vesicles.

the branches do not anastomose, and ultimately they terminate in small arterioles, which supply several adjacent alveoli, each arteriole splitting up into capillaries for *several* air-cells (figs. 152, 153, *v, c*). An efferent vein usually arises at the opposite side of the air-cells, and carries away the purified blood from the capillaries. In their course these veins unite to form the **pulmonary veins**, which, again, are joined in their course by a few small bronchial veins. The veins usually anastomose in the earlier part of their course, whilst the corresponding arteries do not.] Although the capillary plexus is very fine and dense, its sectional area is less than the sectional area of the systemic capillaries, so that the blood-stream in the pulmonary capillaries must be more rapid than that in the capillaries of the body

generally. The pulmonary veins, unlike veins generally, are collectively narrower than the pulmonary artery (water is given off in the lungs), and they have no valves.

[The pulmonary artery contains venous blood, and the pulmonary veins pure or arterial blood].

(B) The **bronchial vessels** represent the nutrient system of the lungs. The **bronchial arteries** (1-3) arise from the aorta (or intercostal arteries) and accompany the bronchi without anastomosing with the branches of the pulmonary artery. In their course they give branches to the lymphatic glands at the hilum of the lung, to the walls of the large blood-vessels (*vasa vasorum*), the pulmonary pleura, the bronchial walls, and the interlobular septa. The blood which issues from their capillaries is returned—*partly* by the pulmonary veins—hence, any considerable interference with the



Fig. 151.

Air-vesicles injected with silver nitrate. *a*, outlines of squamous epithelium; *b*, alveolar wall; *c*, young epithelium cell; *d*, aggregation of young epithelial cells germinating $\times 350$.

pulmonary circulation causes congestion of the bronchial mucous membrane, resulting in a catarrhal condition of that membrane. The greater part of the blood is returned by the **bronchial veins**, which open into the vena azygos, intercostal vein, or superior vena cava. The veins of the smaller bronchi (fourth order onwards) open into the pulmonary veins, and the anterior bronchial also communicate with the pulmonary vein (*Zuckerkanll*).

[The **Pleura**.—Each pleural cavity is distinct, and is a large serous sac, which really belongs to the lymphatic system of the lung. The pleura consists of two layers, **visceral** and **parietal**. The **visceral pleura** covers the lung; the parietal portion lines the wall of the chest, and the two layers of the corresponding pleura are continuous with one another at the root of the lung. The parietal pleura is the thicker, and may readily be separated from the inner surface of the chest. Structurally, the pleura resembles a serous membrane, and consists of a thin layer of fibrous tissue covered by a layer of endothelium. Under this layer, or the pleura proper, is a **deep** or **sub-serous layer** of looser areolar tissue, containing many elastic fibres. The layer of the pleura pulmonalis of some animals, as the guinea-pig, contains a network of non-striped muscular fibres. Over the lung it is also continuous with the interlobular septa.]

[The **Interlobular Septa** (fig. 154, *e*) consist of bands of fibrous tissue separating adjoining lobules, and they become continuous with the peri-bronchial connective tissue entering the lung at its hilum. Thus the fibrous framework of the lung is continuous throughout the lung, just as in other organs. The connection of the sub-pleural fibrous tissue with the connective tissue within the substance of the lung has most important pathological bearings. The interlobular septa contain lymphatics and blood-vessels. The endothelium covering the parietal layer is of the ordinary squamous type, but on the pleura pulmonalis the cells are less flattened,

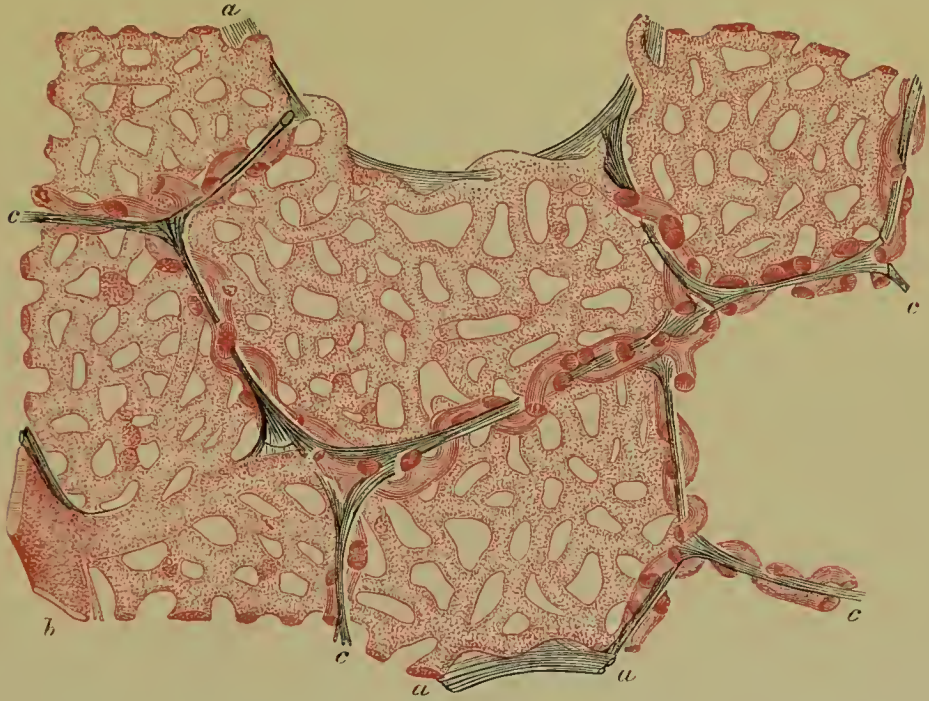


Fig. 152.

Section of the vesicular tissue of a human lung injected from the pulmonary artery; *a, a*, free margins of the alveoli; *b*, small artery; *c, c*, vertical walls of alveoli divided transversely.

more polyhedral, and granular. They must necessarily vary in shape with changes in the volume of the lung, so that they are more flattened when the lung is distended, as during inspiration. The pleura contains many lymphatics, which communicate by means of **stomata** with the pleural cavity.]

[The **Lymphatics** of the lung are numerous, and are arranged in several systems. The various air-cells are connected with each other by very delicate connective tissue, and, according to J. Arnold, in some parts this interstitial tissue presents characters like those of adenoid tissue; so that the lung is traversed by a system of **juice-canals** or "**Saft-canalchen**." In the deep layer of the pleura there is a (*a*) **sub-pleural plexus of lymphatics** partly derived from the pleura, but chiefly from the lymph-canalicular system of the pleural alveoli. Some of these branches proceed to the bronchial glands, but others pass into the interlobular septa, where they join (*b*) the **peri-vascular lymphatics** which arise in the lymph-canalicular system of the alveoli. These trunks, provided with valves, run alongside the pulmonary artery and vein, and in their course they form frequent anastomoses. Special vessels arise within the walls of the bronchi, and occur chiefly in the outer coat of the latter, constituting (*c*) the **peri-bronchial lymphatics**, which anastomose with *b*. The branches of these two sets run towards the bronchial glands.

Not unfrequently (cat) masses of adenoid tissue are found in the course of these lymphatics.] The lymph-canalicular system and the lymphatics become injected, when fine coloured particles are inspired, or are introduced into the air-cells artificially. The pigment particles pass through the semi-fluid cement-substance into the lymph-canalicular system and thence into the lymphatics; or, according to Klein, they pass through actual holes or pores in the cement (p. 185). [This pigmentation is well seen in coal-miner's lung or **anthracosis**, where the particles of carbon pass into and are found in the lymphatics. Sikorski and Küttner showed that pigment reached the lymphatics in this way during life. If pigment, China



Fig. 153.

Semi-diagrammatic representation of the air-vesicles of the lung. *v, v*, blood-vessels at the margins of an alveolus; *c, c*, its blood-capillaries; *E*, relation of the squamous epithelium of an alveolus to the capillaries in its wall; *f*, alveolar epithelium shown alone; *c, e*, elastic tissue of the lung

ink or indigo-carmin, be introduced into a frog's lung, it is found in the lymphatic system of the lung. Ruppert, and also Schotelius, showed that the same result occurred in dogs, after the inhalation of charcoal, cinnabar, or precipitated Berlin blue, and von Ins after the inhalation of silica. Schestopal used China ink and cinnabar suspended in $\frac{3}{4}$ per cent. salt solution.] Excessively fine lymph-canals lie in the wall of the alveoli in the interspaces of the capillaries, and there are slight dilatations at the points of crossing. According to Pierret and Renaut, every air-cell of the lung of the ox is surrounded by a large lymph-space, such as occurs in the salivary glands. When a large quantity of fluid is injected into the lung, it is absorbed with great rapidity; even blood-corpuscles rapidly pass into the lymphatics.

The **superficial lymphatics** of the pulmonary pleura communicate with the pleural cavity by means of free openings or **stomata**, and the same is true of the

lymphatics of the parietal pleura, but these stomata are confined to limited areas over the diaphragmatic pleura. [The lymphatics in the costal pleura occur over the intercostal spaces and not over the ribs (*Dybkowski*).] The large arteries of the lung are provided with lymphatics which lie between the middle and outer coats. [The movements of the lung during respiration are most important factors in moving the lymph onwards in the pulmonary lymphatics. The reflux of the lymph is prevented by the presence of valves.]

Absorption of particles in lungs and pleura.—If blood or China ink be injected into the lungs, the corpuscles are rapidly absorbed from the lungs, but not from the trachea or large bronchi. In the lungs the particles pass between the alveolar epithelium into the interstitial pulmonary tissue, and finally into the peri-bronchial and peri-arterial lymphatics, and from thence to the bronchial lymph-glands. Similar injections into the pleural cavity are absorbed (5–30 minutes) by the costal and mediastinal pleura, but not by the pulmonary pleura.]

[The **nerves** of the lung are derived from the anterior and posterior **pulmonary plexuses** and consist of branches from the vagus and sympathetic, and from certain dorsal nerves (p. 149). They enter the lungs and follow the distribution of the bronchi, several sections of nerve-trunks being usually found in a transverse section of a large bronchial tube. The nerves lie outside the cartilages, and are in close relation with the branches of the bronchial arteries. Medullated and non-medullated nerve-fibres occur in the nerves, which also contain numerous small **ganglia** (*Remak, Klein, Stirling*). In the lung of the calf the ganglia are large. The exact mode of termination of the nerve-fibres within the lung has yet to be ascertained in mammals, but some fibres pass to the bronchial muscle, others to the large blood-vessels of the lung, and it is highly probable that the mucous glands are also supplied with nerve filaments. In the comparatively simple lungs of the frog, nerves with numerous nerve-cells in their course are found (*Arnold, Stirling*), and in the very simple lung of the newt, there are also numerous nerve-cells disposed along the course of the intra-pulmonary nerves. Some of these fibres terminate in the uniform layer of non-striped muscle which forms part of the pulmonary wall in the frog and newt, and others end in the muscular coat of the pulmonary blood-vessel (*Stirling*). The functions of these ganglia are unknown, but they may be compared to the nerve-plexuses existing in the walls of the digestive tract.]

The **Function** of the **non-striped muscle** of the entire bronchial system seems to be to offer a sufficient amount of resistance to increased pressure within the air-passages; as in forced expiration, speaking, singing, blowing, &c. The vagus is the motor nerve for these fibres, and according to Longet, the “lung-tonus” during increased tension depends upon these muscles.

[**Contraction of the Lungs and Bronchi—Effect of Nerves.**—By connecting the interior of a small bronchus with an oncograph (§ 103) in curarised dogs (the thorax being opened), Brown and Roy found that section of one **vagus** causes a marked expansion of the bronchi of the corresponding lung, while stimulation of the peripheral end of a divided vagus causes a powerful contraction of the bronchi of both lungs. Stimulation of the central end of one vagus, the other being intact, also causes a contraction (feeblor) under the same circumstances. Especially in etherised dogs, expansion and not contraction results. If both vagi be divided, no effect is produced by stimulation of the central end of either vagus. It seems plain that the vagi contain centripetal or afferent fibres, which can cause both expansion and contraction of the bronchi. Asphyxia causes contraction provided the vagi are intact, but none if they are divided, although in etherised dogs expansion frequently occurs, while stimulation of the central end of other sensory nerves has very rarely any, or, if any, but a slight, effect on the calibre of the bronchi, so that in the dog the only connection between the cerebro-spinal centres and the bronchi is through the vagi. Sandmaun has confirmed the above observations for rabbits and cats, so that it seems certain that the vagus contains some fibres which dilate and others which cause contraction of the bronchi. Reflex contraction can be brought about by stimulation of the nose and larynx. Williams, Paul Bert, and others showed that the bronchi and lungs are contractile when they are stimulated with electricity. This contractility is very marked in reptilian lungs where there is a well-marked layer of smooth muscle.]

Pathological.—Stimulation of the smooth muscles, whereby a spasmodic narrowing of the

smaller bronchi is produced, may excite asthmatic attacks. If the expiratory blast be interfered with, acute emphysema may take place (*Biernier*).

Chemistry.—In addition to connective, elastic and muscular tissue, the lungs contain lecithin, inosit, uric acid (taurin and leucin in the ox), guanin, xanthin (?), hypoxanthin (dog) soda, potash, magnesium, oxide of iron, much phosphoric acid, also chlorine, sulphuric and silicic acids—in diabetes sugar occurs—in purulent infiltration glycogen and sugar—in renal degeneration urea, oxalic acid, and ammonia salts; and in diseases where decomposition takes place, leucin and tyrosin.

Physical Properties of the Lungs.—The lungs, in virtue of the large amount of elastic tissue which they contain, are highly **elastic**; and when the chest

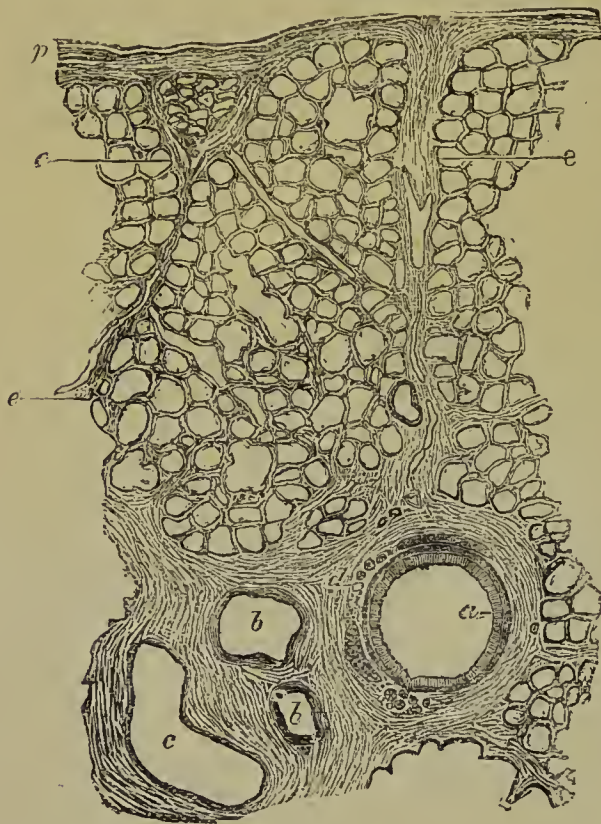


Fig. 154.

Human lung ($\times 50$ and reduced $\frac{1}{2}$). *a*, small bronchus; *b*, *b*, pulmonary artery; *c*, pulmonary vein; *e*, interlobular septa, continuous with the deep layer of the pleura, *p*.

is opened they collapse. If a cannula with a small lateral opening be tied into the trachea of a rabbit's or sheep's lungs, the lungs may be inflated with a pair of bellows, or elastic pump. After the artificial inflation, the lungs, owing to their elasticity, collapse and expel the greater part of the air. As much air remains within the light spongy tissue of the lungs, even after they are removed from the body, a healthy lung floats in water. If the air-cells are filled with pathological fluids or blood, as in certain diseased conditions of the lung (pneumonia), then the lungs or parts thereof may sink in water. The lungs of the foetus, before respiration has taken place, sink in water, but after respiration has been thoroughly established in the child, the lungs float. Hence this **hydrostatic test** is largely used in medico-legal cases, as a test of the child's having breathed. If a healthy lung be squeezed between the fingers, it emits a peculiar and characteristic fine crackling sound, owing to the air within the air-cells. A similar sound is heard on cutting the

vesicular tissue of the lung. The **colour** of the lungs varies much; in a young child it is rose-pink, but afterwards it becomes darker, especially in persons living in towns or a smoky atmosphere, owing to the deposition of granules of carbon. In coal-miners the lungs may become quite black.]

[**Excision of the Lung.**—Dogs recover after the excision of one entire lung, and they even survive the removal of portions of lung affected with tubercle (*Biondi*).]

107. MECHANISM OF RESPIRATION.—The mechanism of respiration consists in an alternate dilatation and contraction of the chest. The dilatation, technically called "expansion," is called **inspiration**, the contraction **expiration**. As the whole external surfaces of both elastic lungs are applied directly, and in an air-tight manner, by their smooth moist pleural investment to the inner wall of the chest, which is covered by the parietal pleura, it is clear that the lungs must

be distended with every dilatation of the chest, and diminished by every contraction thereof. The **movements of the lungs**, therefore, are entirely **passive**, and are dependent on the thoracic movements.

On account of their complete elasticity and their great extensibility, the lungs are able to accommodate themselves to any variation in the size of the thoracic cavity, without the two layers of the pleura becoming separated from each other. As the capacity of the non-distended chest is greater than the volume of the collapsed lungs after their removal from the body, it is clear that the lungs, even in their natural position within the chest, are distended, *i.e.*, they are in a certain state of **elastic tension** (§ 60). The tension is greater the more distended the thoracic cavity, and *vice versâ*. As soon as the pleural cavity is opened by perforation from without, the lungs, in virtue of their elasticity, collapse, and a space filled with air is formed between the surface of the lungs and the inner surface of the thoracic wall (**pneumo-thorax**). The lungs so affected are rendered useless for respiration; hence a double pneumo-thorax causes death.

Pneumo-thorax.—It is also clear that if the pulmonary pleura be perforated from within the lung, air will pass from the respiratory passages into the pleural sac, and also give rise to pneumo-thorax. [Not unfrequently the surgeon is called on to open the chest, say by removing a portion of a rib to allow of the free exit of pus from the pleural cavity. If this be done with proper precautions, and if the external wound be allowed to heal, after a time the air in the pleural cavity becomes absorbed, the collapsed lung tends to regain its original form, and again becomes functionally active.]

Estimation of Elastic Tension.—If a manometer be introduced through an intercostal space into the pleural cavity in a dead subject, we can measure, by means of a column of mercury, the amount of the elastic tension required to keep the lung in its position. This is equal to 6 mm. Hg. in the dead subject, as well as in the condition of expiration. If, however, the thorax be brought into the position of inspiration by the application of traction from without, the elastic tension may be increased to 30 mm. Hg. (*Donders*).

If the glottis be closed and a deep inspiration taken, the air within the lungs must become rarefied, because it has to fill a greater space. If the glottis be suddenly opened, the atmospheric air passes into the lungs until the air within the lungs has the same density as the atmosphere. Conversely, if the glottis be closed, and if an expiratory effort be made, the air within the chest must be compressed. If the glottis be suddenly opened, air passes out of the lungs until the pressure outside and inside the lung is equal. As the glottis remains open during ordinary respiration, the equilibration of the pressure within and without the lungs will take place gradually. During tranquil inspiration there is a slight negative pressure; during expiration a slight positive pressure, in the lungs; the former = 1 mm., the latter 2–3 mm. Hg. in the human trachea (measured in cases of wounds of the trachea). According to J. R. Ewald, however, the values are only 0.1 and 0.13 mm. Hg respectively.

108. QUANTITY OF GASES RESPIRED.—As the lungs within the chest never give out all the air they contain, it follows that only a part of the air of the lungs is changed during inspiration and expiration. The volume of this air will depend upon the depth of the respirations.

COMPLEMENTAL AIR 110	} RESPIRATORY CAPACITY 230 cubic inches.
TIDAL AIR 20	
RESERVE AIR 100	
RESIDUAL AIR 100	

- Hutchinson defined the following:—
- (1) **Residual air** is the volume of air which remains in the chest *after the most complete expiration*. It is = 1230–1640 c.c. [100–130 cubic inches].
 - (2) **Reserve or supplemental air** is the volume of air which can be expelled from the chest *after a normal quiet expiration*. It is = 1240–1800 c.c. [100 cubic inches].
 - (3) **Tidal air** is the volume of air which is taken in and given out at each respiration. It is = 500 cubic centimetres [20 cubic inches. Sometimes it is stated to be 25–30 cubic inches.]
 - (4) **Complemental air** is the volume of air that can be forcibly inspired over and above what is taken in at a normal respiration. It amounts to about 1500 c.c. [100–130 cubic inches].

(5) **Vital Capacity** is the term applied to the volume of air which can be forcibly expelled from the chest after the deepest possible inspiration. It is equal to 3772 c.c. (or 230 cubic inches) for an Englishman (*Hutchinson*), and 3222 for a German (*Haeser*).

Hence, after every quiet inspiration, both lungs contain $(1 + 2 + 3) = 3000$ to 3900 c.cm. [220 cubic inches]; after a quiet expiration $(1 + 2) = 2500$ to 3400 c.cm. [200 cubic inches]. So that about $\frac{1}{6}$ to $\frac{1}{7}$ of the air in the lungs is subject to renewal at each ordinary respiration.

[It is important to remember that the lungs, even after the deepest expiration, always contain a large amount of air. In this way the diffusion of gases between the air in the lungs and the blood-gases can go on continuously, with increase of the process at every inspiration.]

Donders calculated that the entire bronchial system and the trachea contain about 500 e.e. of air.

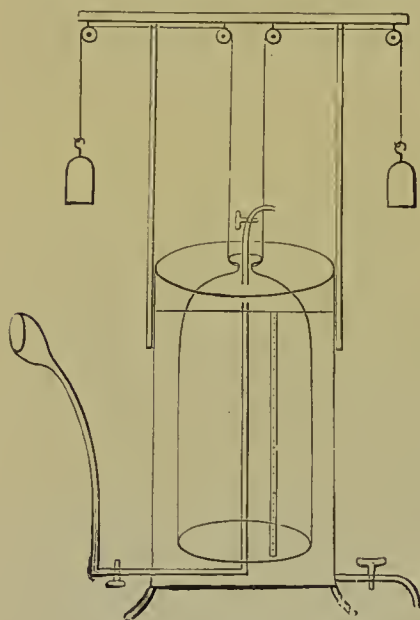


Fig. 155.

Scheme of Hutchinson's spirometer.

Estimation of Vital Capacity.—This was formerly thought to be of great utility, but at the present time not much importance is attached to it, nor is it frequently measured in cases of disease. It is estimated by means of the **spirometer** of Hutchinson, which consists of a graduated cylinder filled with water and inverted like a gasometer over water, and balanced by means of a counterpoise (fig. 155). Into the cylinder a tube projects, and this tube is connected with a mouthpiece. The person to be experimented upon takes the deepest possible inspiration, closes his nostrils, and breathes forcibly into the mouthpiece of the tube. After doing so the tube is closed. The cylinder is raised by the air forced into it, and after the water inside and outside the cylinder is equalised, the height to which the cylinder is raised indicates the amount of air

expired, or the vital or respiratory capacity. In a man of average height, 5 feet 8 inches, it is equal to 230 cubic inches.

The following circumstances affect the vital capacity :—

(1) **The Height.**—Every inch added to the height of persons between 5 and 6 feet gives an increase of the vital capacity = 130 e.c. [8 cubic inches.]

(2) **Body-weight.**—When the body-weight exceeds the normal by 7 per cent. there is a diminution of 37 e.c. of the vital capacity for every kilo. of increase.

(3) **Age.**—The vital capacity is at its maximum at 35; there is an annual decrease of 23.4 e.c. from this age onwards to 65, and backwards to 15 years of age.

(4) **Sex.**—It is less in women than men, and even where there is the same circumference of chest, and the same height in a man and a woman, the ratio is 10 : 7.

(5) **Position and Occupation.**—More air is respired in the erect than in the recumbent position. In the following three categories the preceding group has a vital capacity greater by 200 e.c. than the one following it : (a) soldiers and sailors; (b) hand-workers, compositors; (c) paupers, officials, students (*Arnold*).

(6) **Disease.**—Abdominal and thoracic diseases diminish it.

109. NUMBER OF RESPIRATIONS.—In the adult, the number of respirations varies from 16 to 24 per minute, so that about 4 pulse-beats occur during each respiration. The number of respirations is influenced by many conditions :—

(1) **The Position of the Body.**—In the adult, in the horizontal position, Guy counted 13, while sitting 19, while standing 22, respirations per minute.

(2) **Age.**—Quetelet found the mean number of respirations in 300 individuals to be:—

Year.	Respirations.	Average Number per Minute.	Year.	Respirations.	Average Number per Minute.
0 to 1,	44		20 to 50,	18·7	
5,	26		25 to 30,	16	
15 to 20,	20		30 to 35,	18·1	

(3) **The State of Activity.**—Gorham counted in children of 2 to 4 years of age during standing 32, in sleep 24, respirations per minute. During bodily exertion the number of respirations increases before the heart-beats. [Very slight *muscular* exertion suffices to increase the frequency of the respirations.]

[(4) **The Temperature** of the surrounding medium.—The respirations become more numerous the higher the surrounding temperature, but this result only occurs when the actual temperature of the blood is increased, as in fever.]

(5) **Digestion.**—There is a slight variation during the course of the day, the increase being most marked after mid-day dinner (*Vierordt*).

(6) The **Will** can to a certain extent modify the number and also the depth of the respirations, but after a short time the impulse to respire overcomes the voluntary impulse.

(7) The **Gases of the Blood** have a marked effect, and so has the heat of the blood in fever.]

[(8) In **Animals**—

Mammals.		Per Min.			Per Min.			Per Min.
Tiger,	.	6	Rabbit,	.	55	Pigeon,	.	30
Lion,	.	10	Rat (waking),	.	210	Siskin,	.	100
Jaguar,	.	11	Rat (asleep),	.	100	Canary,	.	18
Panther,	.	18	Rhinoceros,	.	6-10	Reptiles.		
Cat,	.	24	Hippopotamus,	.	1			
Dog,	.	15	Horse,	.	10-12	Snake,	.	5
Dromedary,	.	11	Ass,	.	70	Tortoise,	.	12
Giraffe,	.	8-10	Birds.			Invertebrata.		
Ox,	.	15-18	Condor,	.	6	Crab,	.	12
Squirrel,	.	70	Sparrow,	.	90	Mollusea,	.	14-16
						(P. Bert).]		
						Fish.		
						Raja,	.	50
						Torpedo,	.	51

[(9) **In Disease.**—The number may be greatly increased from many causes, *e.g.*, in fever, pleurisy and pneumonia, some heart diseases, or in certain cases of alteration of the blood, as

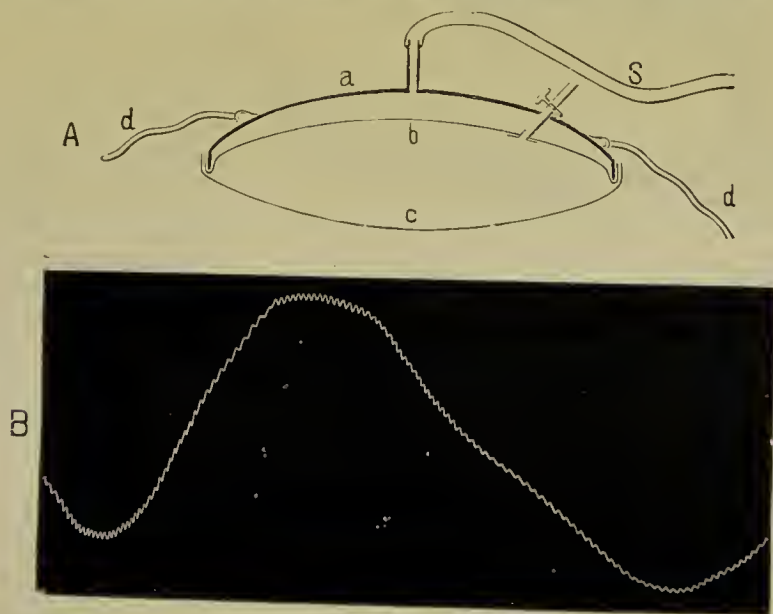


Fig. 156.

A, Brondgeest's tambour for registering the respiratory movements. *b, c*, inner and outer caoutchouc membranes; *a*, the capsule; *d, d'*, cords for fastening the instrument to the chest; *S*, tube to the recording tambour. B, normal respiratory curve obtained on a vibrating plate [each vibration = 0·01613 sec.].

in anæmia; and diminished where there is pressure on the respiratory centre in the medulla in coma. It is important to note the ratio of pulse-beats to respirations.]

110. TIME OCCUPIED BY THE RESPIRATORY MOVEMENTS.—The time occupied in the various phases of a respiration can only be accurately ascertained by obtaining a curve or **pneumatogram** of the respiratory movements by means of recording apparatus.

Methods.—The graphic method can be employed in three directions:—(1) To record the movements of individual parts of the chest-wall.

(1) Vierordt and C. Ludwig transferred the movements of a part of the chest-wall to a lever which inscribed its movements upon a revolving cylinder. Riegel (1873) constructed a “double-stethograph” on the same principle. This instrument is so arranged that one arm of the lever may be applied in connection with the healthy side of a person’s chest, and the other on the diseased side. In the case of animals placed on their backs, Snellon introduced a long needle vertically through the abdominal walls into the liver. Rosenthal opened the abdomen and applied a lever to the under surface of the diaphragm, and thus registered its movements (**Phrenograph**).

(2) An air-tambour, such as is used in Brondgeest’s pansphygmograph (fig. 156, A), may be employed. It consists of a brass vessel, *a*, shaped like a small sancer. The mouth of the brass vessel is covered with a double layer of caoutchouc membrane, *b*, *c*, and air is forced in between the two layers until the external membrane bulges outwards. This is placed on the chest, and the apparatus is fixed in position by means of the bands, *d*, *e*. The cavity of the tambour communicates by means of a caoutchouc tube, *s*, with a recording tambour, which inscribes its movements upon a revolving cylinder. Every dilatation of the chest compresses the membrane, and thus the air within the tambour is also compressed. [A somewhat similar apparatus is used by Burdon-Sanderson, and called a “recording-stethograph.” By its movements of the corresponding points on opposite sides of the chest can be investigated.] A cannula or œsophageal sound may be introduced into that portion of the œsophagus which lies in the chest, and a connection established with Marey’s tambour (Rosenthal). [This method also enables one to measure the intrathoracic pressure (p. 209).]

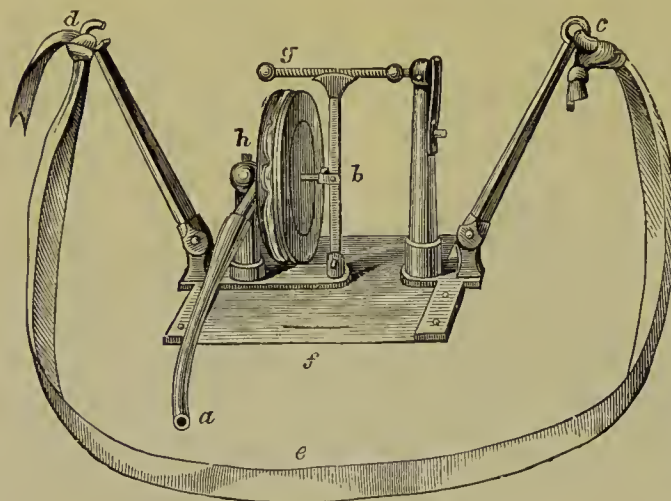


Fig. 157.

Marey's stethograph.

fied by P. Bert and the more modern form (fig. 157). A tambour (*h*) is fixed at right angles to a thin elastic plate of steel (*f*). The aluminium disc on the caoutchouc of the tambour is attached to an upright (*b*), whose end lies in contact with a horizontal screw (*g*). Two arms (*d*, *e*) are attached to opposite sides of the steel plate, and to them the belt (*c*) which fastens the instrument to the chest is attached. When the chest expands, these two arms are pulled asunder, the steel plate is bent, and the tambour is affected, and any movement of the tambour is transmitted to a registering tambour by the air in the tube (*a*).]

Movements of the Diaphragm.—[The phases of respiration have been studied in animals by Kronecker and Marekwald by inserting the spoon-shaped end of a probe-like instrument through the abdominal wall, and between the liver and the diaphragm. From the pointed end of this instrument a thread passes over a pulley to be attached to a lever recording its movements on a drum.]

(2) To record variation in volume of the thorax or of the respired gases.

For this purpose E. Hering secures the animal, and places it in a tight box provided with two openings in its side; one hole contains a tube, which is connected to a cannula tied into the transversely divided trachea of the animal, so that respiration can go on undisturbed. In the other orifice is fixed a water-manometer provided with a swimmer arranged to write on a recording surface. Gad registers graphically the respired air by means of a special apparatus, the **æro-plethysmograph**; the expired air raises a very light and carefully equiposed box placed over water. As it is raised, it moves a writing-style. During inspiration the box sinks.

(3) To record the rate at which the respiratory gases are exchanged.

If the trachea of an animal, or the mouth of a man (the nostrils being closed), be connected with a tube like that of the dromograph (fig. 156), then during inspiration and expiration the pendulum will be moved to and fro by the air, and the movements of the penulum can be registered. [Some years ago an instrument, called the "**Anapnograph**" was constructed on this principle.]

The curve (fig. 156, B) was obtained by placing the tambour of a Brondgeest's pansphygmograph upon the xiphoid process, and recording the movement upon a plate attached to a vibrating tuning-fork. The *inspiration* (ascending limb) begins with moderate rapidity, is accelerated in the middle, and towards the end again becomes slower. The *expiration* also begins with moderate rapidity, is then accelerated, and becomes much slower at the latter part, so that the curve falls very gradually.

Inspiration is slightly shorter than Expiration.—According to Sibson, the ratio for an adult is as 6 to 7; in women, children, and old people, 6 to 8 or 6 to 9. Vierordt found the ratio to be 10 to 14.1 (to 24.1); J. R. Ewald, 11 to 12. [For all practical purposes the following represents the ratio—

Inspiration : Expiration :: 5 : 6.]

It is only occasionally that cases occur where inspiration and expiration are equally long, or where expiration is shorter than inspiration. When respiration proceeds quietly and regularly, there is usually *no pause* (complete rest of the chest-walls) *between the inspiration and expiration*. The very flat part of the expiratory curve has been wrongly regarded as due to a pause. Of course, we may make a voluntary pause between two respirations, or at any part of a respiratory act.

Some observers, however, have described a pause as occurring between the end of expiration and the beginning of the next inspiration (expiration pause), and also another pause at the end of inspiration (inspiration pause). The latter is always of very short duration, and considerably shorter than the former. During very deep and slow respiration, there is usually an expiration pause, while it is almost invariably absent during rapid breathing. An inspiration pause is always absent under normal circumstances, but it may occur under pathological conditions.

In certain parts of the respiratory curve slight irregularities may appear, which are sometimes due to vibrations communicated to the thoracic walls by vigorous heart-beats (fig. 158).

The "**type of respiration**" may be ascertained by taking curves from various parts during the respiratory movements. Hutchinson showed that, in the female, the thorax is dilated chiefly by raising the sternum and the ribs (*Respiratio costalis*), while in man it is caused chiefly by a descent of the diaphragm (*Respiratio diaphragmatica* or *abdominalis*). In the former, there is the so-called "**costal type**," in the latter the "**diaphragmatic** or **abdominal type**."

This difference in the type of respiration in the sexes occurs only during normal quiet respiration. During deep and **forced respiration**, in both sexes the dilatation of the chest is caused chiefly by raising the chest and the ribs. In man, the epigastrium may be pulled in sooner than it is protruded. During **sleep**, the type of respiration in both sexes is thoracic, while at the same time the inspiratory dilatation of the chest precedes the elevation of the abdominal wall (*Mosso*). It is not determined whether the costal type of respiration in the female depends upon the constriction of the chest by corsets or other causes (*Sibson*), or whether it is a natural adaptation to the child-bearing function in women (*Hutchinson*). Some observers maintain that the difference of type is quite distinct, even in sleep, when all constrictions are removed; and that similar differences are noticeable in young children. This is denied by others, while a third class of observers hold that the costal type occurs in children of both sexes, and they ascribe as a cause the greater flexibility of the ribs of children and women, which permits the muscles of the chest to act more efficiently upon the ribs.

111. PATHOLOGICAL.—[**Examination of the Lungs.**—The same methods that are applicable to the heart apply here also, viz.—

- I. Inspection (including Mensuration).
- II. Palpation (including vocal fremitus).
- III. Percussion (including sense of resistance); and
- IV. Auscultation (including vocal resonance).]

[By **inspection** we may determine the presence of symmetrical or unilateral alterations in the shape of the chest, the presence of bulging or flattening at one part, and variations in the movement of the chest-walls. By **palpation**, the presence or absence, character, seat, and extent of any movements are more carefully examined. But we may also study what is called **vocal fremitus** (§ 117), **Percussion** (§ 114), **Auscultation** (§ 116).]

[In investigating the respiratory movements, we should observe (1), the **frequency** (§ 109); (2), the **type** (§ 110); (3), the **nature**, character, and extent of the movements, noting also whether they are accompanied by pain or not (§ 110); (4), the **rhythm**.]

I. Changes in the mode of Movement.—In persons suffering from disease of the respiratory organs, the dilatation of the chest may be diminished (to the extent of 5 or 6 cm.) on *both* sides or only on *one* side. In affections of the apex of the lung (in phthisis), the sub-normal expansion of the upper part of the wall of the chest may be considerable. *Retraction* of the soft parts

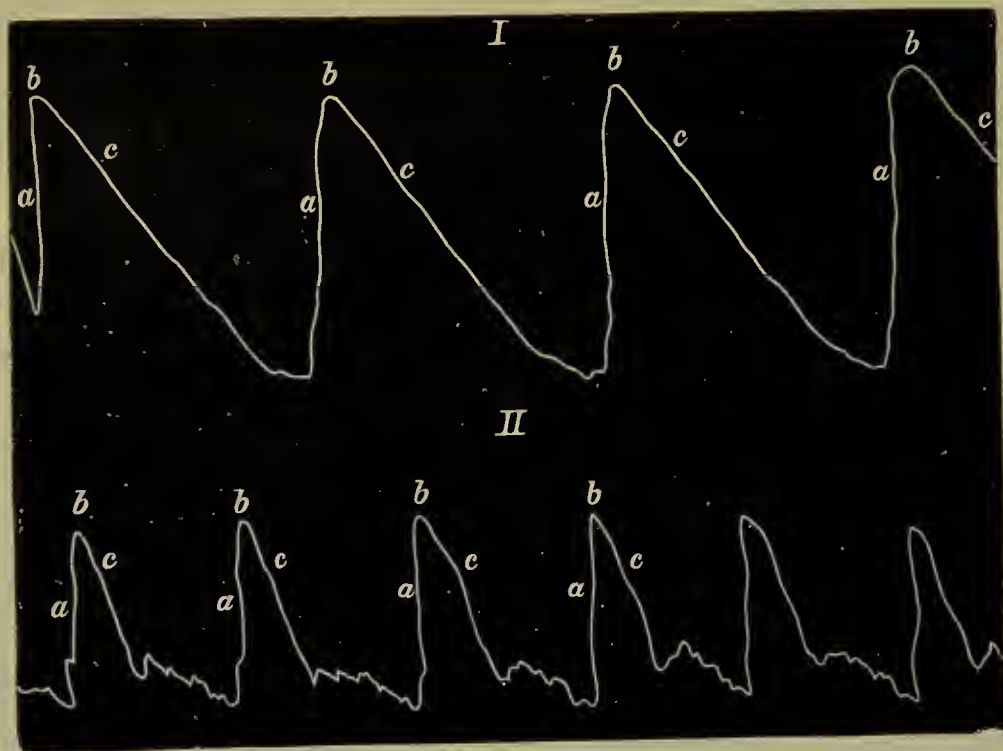


Fig. 158.

Pneumatograms obtained by means of Riegel's stethograph. I, normal curves; II, curve from a case of emphysema; *a*, ascending limb; *b*, apex; *c*, descending limb of the curve. The small elevations are due to the cardiac impulse.

of the thoracic wall, the xiphoid process, and the parts where the lower ribs are inserted, occurs in cases where air cannot freely enter the chest during inspiration, *e.g.*, in narrowing of the larynx; when this retraction is confined to the upper part of the thoracic wall, it indicates that the portion of the lung lying under the part so affected is less extensible and diseased.

Harrison's Groove.—In persons suffering from chronic difficulty of breathing, and in whom, at the same time, the diaphragm acts energetically, there is a slight groove, which passes horizontally outwards from the xiphoid cartilage, caused by the pulling in of the soft parts and corresponding to the insertion of the diaphragm.

The duration of inspiration is lengthened in persons suffering from narrowing of the trachea or larynx; expiration is lengthened in cases of dilatation of the lung, as in emphysema, where all the expiratory muscles must be brought into action (fig. 158. II).

II. Variations in the Rhythm.—When the respiratory apparatus is much affected, there is either an increase or a deepening of the respirations, or both. When there is great difficulty of breathing, this is called **dyspnœa**.

Causes of Dyspnœa.—(1) Limitation of the exchange of the respiratory gases in the blood due to—(*a*) diminution of the respiratory surface (as in some diseases of the lungs); (*b*) narrowing of the respiratory passages, [when a child sucks, it breathes exclusively through the nose, hence catarrhal conditions of the nasal mucous membrane are fraught with danger to

the child]; (c) diminution of the red blood-corpuscles; (d) disturbances of the respiratory mechanism (e.g., due to affections of the respiratory muscles or nerves, or painful affections of the chest-wall); (e) impeded circulation through the lungs due to various forms of heart-disease. (2) **Heat-dyspnœa.**—The frequency of the respirations is increased in *febrile conditions*. The warm blood acts as a direct irritant of the respiratory centre in the medulla oblongata, and raises the number of respirations to 30–60 per minute (“Heat-dyspnœa”). If the carotids be placed in warm tubes, so as to heat the blood going to the medulla oblongata, the same phenomena are produced (§ 368).]

[**Orthopnœa.**—Sometimes the difficulty of breathing is so great that the person can only respire in the erect position, *i.e.*, when he sits or is propped up in bed. This occurs frequently towards the close of some heart affections, notably in mitral lesions; dropsical conditions, especially of the cavities, may be present.]

Cheyne-Stokes' Phenomenon.—This remarkable phenomenon occurs in certain diseases, where the normal supply of blood to the brain is altered, or where the quality of the blood itself is altered, *e.g.*, in certain affections of the brain and heart, and in uræmic poisoning. Respiratory pauses of one-half to three-quarters of a minute alternate with a short period ($\frac{1}{2}$ – $\frac{3}{4}$ min.) of increased respiratory activity, and during this time 20–30 respirations occur. The respirations constituting this “series” are shallow at first; gradually they become deeper and deeper, and finally become shallow or superficial again. Then follows the pause, and thus there is an alternation of pauses and series (or groups) of modified respirations.

[Fig. 159 shows a tracing of the respiratory movements. The increase from shallow to deeper respirations is sometimes called the “ascending phase,” and the reverse the “descending phase.” As will be seen, the pause occupies somewhat less than the half of one period. Dixon Mann has recorded a case where this

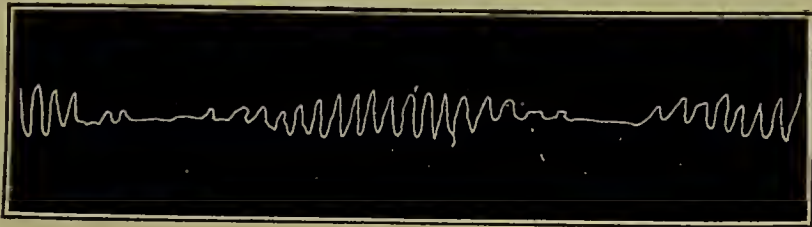


Fig. 159.

Tracing of Cheyne-Stokes' breathing (*Gibson*).

phenomenon lasted for more than a year.] During the pause, the pupils are contracted and inactive; and when the respirations begin, they dilate and become sensible to light; the eyeball is moved as a whole at the same time. [Mann found that the pupils did not contract during the pause, nor was there any change in their size on the return of breathing.] Hein observed that consciousness was abolished during the pause, and that it returned when respiration commenced.

Causes.—Luciani and Rosenbach regard variations in the excitability of the respiratory centre as the cause of the phenomenon, which they compare with the periodic contraction of the heart (§ 58). The excitability of the respiratory centre is lowest during the pause. They observed this phenomenon after injury to the medulla oblongata above the respiratory centre, and after apnœa produced in animals deeply narcotised with opium, and in the last stages of asphyxia, during respiration in a closed space. During hibernation, this mode of respiration is normal in *Myoxus*, the hedgehog, and the caiman.

Periodic Respiration.—If frogs be kept under water, or if the aorta be clamped, after several hours they become passive. If they be taken out of the water, or if the clamp be removed from the aorta, they gradually recover and always exhibit the Cheyne-Stokes' phenomenon. In such frogs the blood-current may be arrested temporarily, while the phenomenon itself remains (*Sokolow and Luchsinger*). If the blood-current be arrested by ligature of the aorta, or if the frogs be bled, the respirations occur in groups. This is followed by a few single respirations, and then the respiration ceases completely. During the pause between the periods, mechanical stimulation of the skin causes the discharge of a group of respirations (*Siebert and Langendorff*).

Action of Drugs.—Muscarin, digitalin, curare, chloral, sulphuretted hydrogen, and the poison of many infectious diseases (typhus, diphtheria, scarlet fever) may also cause periodic respiration [which is not due to the action of these drugs on the heart].

Periodic respiration without any variation in the size of the individual respirations—the so-called “*Biot’s respiration*”—occurs normally during sleep. While the nervous system as it were strives to rest, and thus forgets the respiration, the organism does not observe the short pauses (*Mosso*). [There is a periodic increase or decrease in the depth of the respiration, especially in old people and children, even to the extent of the respiration becoming “remittent,” or even “intermittent,” for a period of 30 sec. during sleep. During periodic respiration the action of the several respiratory muscles does not coincide. As a rule, one respires more than is required by the organism. *Mosso* calls this “*luxus-respiration*.”] Periodic irregularities in the respiration are often of reflex origin (*Knoll*).

112. GENERAL VIEW OF THE RESPIRATORY MUSCLES.

(A) Inspiration.

I. During Ordinary Inspiration.

1. The diaphragm (*Nervus phrenicus*).
2. The Mm. levatores costarum longi et breves (*Rami posteriores Nn. dorsalium*).
3. The Mm. intercostales externi et intercartilaginei (*Nn. intercostales*).

[Ordinary inspiration, therefore, is both diaphragmatic and costal, *i.e.*, it is essentially a muscular act brought about under the influence of the central nervous system, by a series of co-ordinated muscular movements. The diaphragm contracts, and the ribs are raised, at least all except the first. The ribs are raised by the levatores costarum, and the external and internal intercostal muscles (p. 201).]

II. During Forced Inspiration.

(a) Muscles of the Trunk.

1. The three Mm. scaleni (*Rami musculares of the plexus cervicalis et brachialis*).
2. M. sternocleidomastoideus (*Ram. externus N. accessorii*).
3. M. trapezius (*R. externus N. accessorii et Ram. musculares plexus cervicalis*).
4. M. pectoralis minor (*Nn. thoracici anteriores*).
5. M. serratus posticus superior (*N. dorsalis scapulae*).
6. Mm. rhomboidei (*N. dorsalis scapulae*).
7. Mm. extensores columnae vertebralis (*Ram. posteriores nervorum dorsalium*).
- [8. Mm. serratus anticus major (*N. thoracicus longus*). ??]

(b) Muscles of the Larynx.

1. M. sternohyoideus (*Ram. descendens hypoglossi*).
2. M. sternothyroideus (*Ram. descendens hypoglossi*).
3. M. crico-arytaenoides posticus (*N. laryngeus inferior vagi*).
4. M. thyreo-arytaenoides (*N. laryngeus inferior vagi*).

(c) Muscles of the Face.

1. M. dilatator narium anterior et posterior (*N. facialis*).
2. M. levator alae nasi (*N. facialis*).
3. The dilators of the mouth and nares, during forced respiration, [“gasping for breath”] (*N. facialis*).

(d) Muscles of the Pharynx.

1. M. levator veli palatini (*N. facialis*).
2. M. azygos uvulae (*N. facialis*).
3. According to Garland, the pharynx is always narrowed.

[Or, classified according to their action, the auxiliary muscles of forced inspiration

are those that elevate the ribs directly or indirectly, or fix the lower jaw, so that muscles attached to the hyoid bone can act (*Rutherford*).

<i>The hyoid bone is raised by</i>	{ Mylo-hyoid. Genio-hyoid. Stylo-hyoid. Digastric.
<i>The sternum is raised by</i>	{ Sterno-mastoid. Sterno-hyoid. Sterno-thyroid. Thyro-hyoid.
<i>The upper ribs are raised by]</i>	{ Scaleni. Cervicalis ascendens. Serratus posticus superior.
<i>The shoulder girdle is raised and drawn backwards by</i>	{ Trapezius. Levator anguli scapulæ. Rhomboides major. minor.
<i>The following muscles pull on the ribs and tend to approach them to the raised shoulder girdle</i>	{ Pectoralis major. minor. Subclavius. Serratus magnus.]

(B) Expiration.

I. During Ordinary Respiration.

The thoracic cavity is diminished by the *weight* of the chest-wall, the *elasticity* of the lungs, costal cartilages, and abdominal wall and abdominal contents.

[Ordinary expiration, therefore, is non-muscular, and the act is a purely passive one.]

II. During Forced Expiration.

The Abdominal Muscles.

1. The abdominal muscles [including the obliquus externus and internus, and transversalis abdominis] (*Nn. abdominis interni anteriores e nervis intercostalibus*, 8-12).

2. Mm. intercostales interni, so far as they lie between the osseous parts of the ribs, and the Mm. infracostales (*Nn. intercostales*).

3. M. triangularis sterni (*Nn. intercostales*).

4. M. serratus posticus inferior. (*Ram. externi nerv. dorsalium*).

5. M. quadratus lumborum (*Ram. muscular e plexu lumbali*).

6. Rectus abdominis (*Nn. intercostales*, 7-12).

7. Levator ani (*Nn. sacrales*, 3-4).

<i>[The abdominal contents are compressed and forced against the diaphragm by</i>	{ Obliquus externus. internus. Transversus abdominis. Levator ani. Rectus abdominis.
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<i>The ribs are depressed by</i>	{ Rectus abdominis. Quadratus lumborum. Serratus posticus inferior. Triangularis sterni.]
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113. ACTION OF THE INDIVIDUAL RESPIRATORY MUSCLES.—(A) Inspiration.—(1) The Diaphragm arises from the cartilages and the adjoining osseous parts of the lower six ribs

(costal portion), by two thick processes or *erura*, from the upper three or four lumbar vertebrae, and a sternal portion from the back of the ensiform process. It represents an **arched double cupola** or dome-shaped partition, directed towards the chest; in the larger concavity on the right side lies the liver, while the smaller arch on the left side is occupied by the spleen and stomach. During the passive condition, these viscera are pressed against the under surface of the diaphragm by the elasticity of the abdominal walls, and by the intra-abdominal pressure, so that the arch of the diaphragm is pressed upwards into the chest. The elastic traction of the lungs also aids in producing this result. The greater part of the upper surface of the central tendon of the diaphragm is united to the pericardium. The part on which the heart rests, and which is perforated by the inferior vena cava (foramen quadrilaterum) is the deepest part of the middle portion of the diaphragm during the passive condition.

Action of the Diaphragm.—When the diaphragm contracts, both arched portions become flatter, and the chest is thereby elongated from above downwards. In this act, the lateral muscular parts of the diaphragm pass from an arched condition into a flatter form (fig. 160), and during a forced inspiration the lowest

lateral portions, which during rest are in contact with the chest-wall, become separated from it. The middle of the central tendon where the heart rests, (fixed by means of the pericardium and inferior vena cava), takes no share in this movement, especially in ordinary quiet breathing, but during the deepest inspiration it sinks somewhat.



Fig. 160.

Sagittal section through the second rib on the right side. When the arched muscular part of the diaphragm contracts, a wedge-shaped space, with its apex downwards, is formed around the circumference of the lower part of the chest.

as in the dog, section of these nerves does not produce death rapidly.] The phrenic nerve contains some sensory fibres for the pleura, pericardium, and a portion of the diaphragm. [Ganglionic cells have been found in the course of the inter-muscular fibres of the phrenics.] The contraction of the diaphragm is not to be regarded as a "simple muscular contraction," since it lasts 4 to 8 times longer than a simple contraction; it is rather a short tetanic contraction, which we may arrest in any stage of its activity, without bringing into action any antagonistic muscles (*Kronecker and Marckwald*).

(2) **The Elevation of the Ribs.**—The ribs at their vertebral ends (which lie much higher than their sternal ends) are united by means of joints by their heads and tubercles to the bodies and transverse processes of the vertebrae. A horizontal axis can be drawn through both joints, around which the ribs can rotate upwards and downwards. If the axis of rotation of each pair of ribs be prolonged on both sides until they meet in the middle line, the angles so formed are greatest above (125°), and smallest below (88°). Owing to the ribs being curved, we can imagine a plane which, in the passive (expiratory) condition of the chest, has a slope from behind and inwards to the front and outwards. If the ribs move on their axis of rotation, this plane becomes more horizontal, and the thoracic cavity is increased in its transverse diameter. As

Undoubtedly, the diaphragm is the most powerful agent in increasing the cavity of the chest. Brücke believes that in addition to increasing the length of the thoracic cavity from above downwards, it also increases the transverse diameter of the lower part of the chest. It presses upon the abdominal viscera from above, and strives to press these outwards, thus tending to push out the adjoining thoracic wall. If the contents of the abdomen are removed from a living animal, every time the diaphragm contracts the ribs are drawn inwards. This, of course, hinders the chest from becoming wider below, hence the presence of the abdominal viscera seems to be necessary for the normal activity of the diaphragm. Every contraction of the diaphragm, by increasing the intra-abdominal pressure, favours the venous blood-current in the abdomen towards the vena cava inferior.

Phrenic Nerve.—The immense importance of the diaphragm as the *great inspiratory muscle* is proved by the fact that, after both phrenic nerves (third and fourth cervical nerves) are divided, death occurs in some animals. [In animals where the intercostal muscles play a large part in the act of inspiration,

the axis of rotation of the upper ribs runs in a more frontal, and that of the lower ribs in a more sagittal direction, the elevation of the upper ribs causes a greater increase from before backwards, and the lower ribs from within outwards (as the movements of ribs which are directed downwards are vertical to the axis). The costal cartilages undergo a slight tension at the same time, which brings their elasticity into play.

Changes in the Chest.—All inspiratory muscles which act directly upon the chest-wall do so by raising the ribs:—(a) When the ribs are raised, the intercostal spaces are widened. (b) When the upper ribs are raised, all the lower ribs and the sternum must be elevated at the same time, because all the ribs are connected with each other by means of the soft parts of the intercostal spaces. (c) During inspiration, there is an elevation of the ribs and a dilatation of the intercostal spaces. (The lowest rib is an exception: during forced respiration, at least, it is drawn downwards.) (d) If, on a preparation of the chest, the ribs be raised as in inspiration, we may regard all those muscles as elevators of the ribs, whose origin and insertion become approximated. Every one is agreed that the *scaleni* and *levator costarum longi et breves*, the *serratus posticus superior*, are inspiratory muscles. These are the most important inspiratory muscles which act upon the ribs.

Intercostal Muscles.—With regard to the action of the intercostal muscles, there is a great difference of opinion. According to the above experiment, the external intercostals and the intercartilaginous parts of the internal intercostals act as inspiratory muscles, whilst the remaining portions of the internal intercostals (as far as they are covered by the external) are elongated when the ribs are raised, while they shorten when the chest-wall descends. A muscle shortens only during its activity. The internal intercostals were regarded by Hamberger as depressors of the ribs or expiratory muscles.

In fig. 161, I, when the rods, *a* and *b* (which represent the ribs), are raised, the intercostal space must be widened ($ef > cd$). On the opposite side of the figure, it is evident that when the rods are raised, the line, *g h*, is shortened ($ik < gh$, direction of the external intercostals) *l m* is lengthened ($lm < on$, direction of internal intercostals). Fig. 161, II, shows, that when the ribs are raised, the intercartilaginei, indicated by *g h*, and the external intercostals, indicated by *l k*, are shortened. When the ribs are raised, the position of the muscular fibres is indicated by the diagonal of the rhomb becoming shorter.

The mode of action of the intercostal muscles is an old story, Galen (131–203 A.D.) regarding the externals as inspiratory, the internals as expiratory. Hamberger (1727) accepted this proposition, and considered the intercartilaginei also as inspiratory. Haller looked upon both the external and internal intercostals as inspiratory, while Vesalius (1540) regarded both as expiratory. Lauderer, observing that the upper two or three intercostal spaces became narrower during inspiration, regarded both as active during inspiration and expiration. They keep one rib attached to the other, so that their action is to transmit any strain put upon them to the wall of the chest. On this view they will be in action, even when the distance between their points of attachment becomes greater. Landois regards the external intercostals and intercartilaginei as active *only* during inspiration, the internal intercostals *only* during expiration.

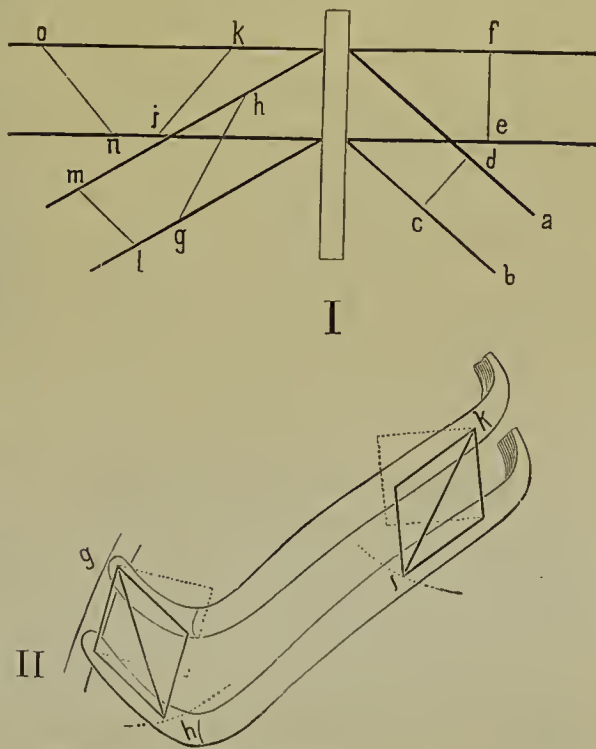


Fig. 161.

Scheme of the action of the intercostal muscles.

Martin and Hartwell exposed the internal intercostals, and observed whether they contracted along with the diaphragm, or whether the contractions of these two muscles alternate. As the result of their experiments, they conclude that "the internal intercostal muscles are expiratory throughout their whole extent, at least in the dog and cat; and that in the former animal they are almost 'ordinary' muscles of respiration, while in the latter they are 'extraordinary' respiratory muscles." Landois is of opinion that the *chief* action of these muscles is not to raise or depress the ribs, but rather that the external intercostals and the intercartilaginei offer resistance to the inspiratory dilatation of the intercostal spaces, and to the simultaneously increased elastic tension of the lungs. The internal intercostals act during powerful expiratory efforts, (*e.g.*, coughing), and oppose the distention of the lungs and chest caused by this act. Unless muscles were present to resist the uninterrupted tension and pressure, the intercostal substance would become so distended that respiration would be impossible. [According to Rutherford, the internal intercostals are probably muscles of inspiration.]

The **Pectoralis minor** and (**Serratus anticus major**) can only act as elevators of the ribs when the shoulders are fixed, partly by the rhomboidei, and partly by fixing the shoulder-joint and supporting the arms, as is done instinctively by persons suffering from breathlessness.

(3) **Muscles acting on the Sternum, Clavicle, and Vertebral Column.**—When the head is fixed by the muscles of the neck, the sternocleidomastoid raises the manubrium sterni and the sternal end of the clavicle, so that the thorax is raised and thereby dilated. The scaleni also aid in this act. The clavicular portion of the trapezius may act in a similar although less energetic manner. When the *vertebral column is straightened*, it causes an elevation of the upper ribs, and a dilatation of the intercostal spaces which aid inspiration. During deep respiration, the straightening of the vertebral column takes place involuntarily.

(4) **Laryngeal Movements.**—During laboured respiration, with every inspiration, the *larynx descends* and the glottis is opened. At the same time the palate is raised, so as to permit a free passage to the air entering through the mouth.

(5) **Facial Movements.**—During laboured respiration, the facial muscles are involved; there is an inspiratory dilatation of the nostrils (well marked in the horse and rabbit). When the need for respiration is very great, the mouth is gradually widened, and the person as it were gasps for breath. During expiration, the muscles that are active during (4) and (5) relax, so that a position of equilibrium is established without there being any active expiratory movement to counteract the inspiratory movement. During inspiration the pharynx becomes narrow (*Garland*).

(B) **Expiration.**—Ordinary expiration occurs without the aid of muscles, owing to the **weight of the chest-wall**, which tends to fall into its normal position from the position to which it was raised during inspiration. This is aided by the **elasticity** of the various parts of the chest. When the costal cartilages are raised, which is accompanied by a slight rotation of their lower margins from below forwards and upwards, their elasticity is called into play. As soon, therefore, as the inspiratory forces cease, the costal cartilages return to their normal position, *i.e.*, the position of expiration, and tend to untwist themselves; at the same time, the **elasticity of the distended lungs** draws upon the thoracic walls and the diaphragm. Lastly, the **tense and elastic abdominal walls**, which, in man chiefly, are stretched and pushed forward, tend to return to their non-distended passive condition when the **abdominal viscera** are relieved from the pressure of the contracted diaphragm. (When the position of the body is reversed, the action of the weight of the chest is removed, but in place of it there is the weight of the viscera, which press upon the diaphragm.)

The **abdominal muscles** [obliquus internus and externus, rectus abdominis, transversalis abdominis and levator ani] are always active during laboured respiration. They act by diminishing the abdominal cavity, and they press the abdominal contents upwards against the diaphragm. When they act simultaneously, the abdominal cavity is diminished throughout its whole extent. The **triangularis**

sterni depresses the sternal ends of the united cartilages and bones, from the third to sixth ribs downwards; and the **serratus posticus inferior** depresses the lowest four ribs, causing the others to follow. It is aided by the **quadratus lumborum**, which depresses the last rib. According to Henle, the serratus posticus inferior fixes the lower ribs for the action of the slips of the diaphragm inserted into them, so that it acts during inspiration. According to Landerer, the downward movement of the ribs in the lower part of the thorax dilates the chest.

In the erect position, when the vertebral column is fixed, deep inspiration and expiration naturally alter the position of the **centre of gravity**, so that during inspiration, owing to the protrusion of the thoracic and abdominal walls, the centre of gravity lies somewhat more to the front. Hence, with each respiration there is an involuntary balancing of the body. During very deep inspiration, the accompanying straightening of the vertebral column and the throwing backwards of the head compensate for the protrusion of the anterior walls of the trunk.

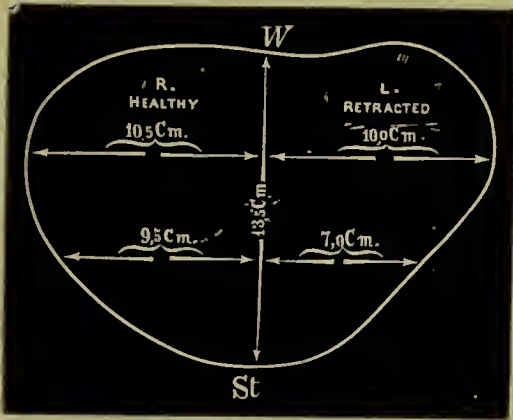


Fig. 162.

Cyrtometer curve. Left side of the chest retracted in a girl aged twelve.

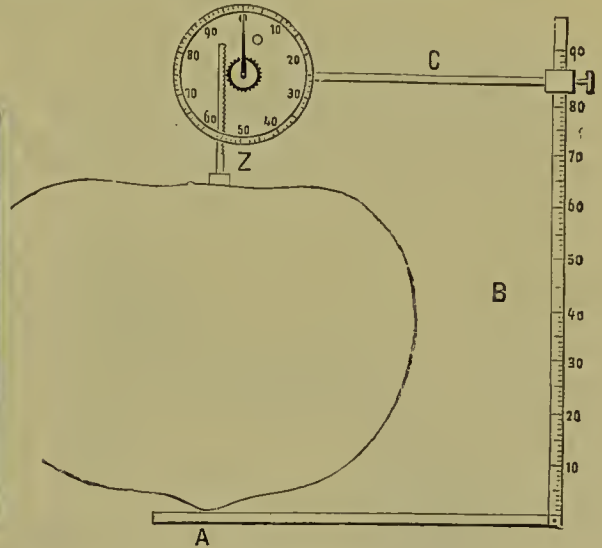


Fig. 163.

Sibson's thoracometer.

114. RELATIVE DIMENSIONS OF THE CHEST.—The diameter of the chest is ascertained by means of callipers; the circumference with a flexible centimetre or other measure.

In strong men, the **circumference** of the upper part of the chest (immediately under the arms) is 88 centimetres (34.3 inches), in females 82 centimetres (32 inches); at the level of the ensiform process 82 centimetres (32 inches) and 78 centimetres (30.4 inches) respectively. [In health the chest expands from $1\frac{1}{2}$ to 5 inches during forced inspiration.] When the arms are placed horizontally, during moderate expiration, the circumference immediately under the nipple and the angles of the scapulæ is equal to half the length of the body; in man 82, and during deep inspiration 89 centimetres. The circumference at the level of the ensiform cartilage is 6 centimetres less. In old people, the circumference of the upper part of the chest is diminished, so that the lower part becomes the wider of the two. The right half of the chest is usually slightly larger than the left half, owing to the greater development of the muscles on that side. The **long diameter** of the chest—from the clavicle to the margin of the lowest rib—varies very much.

The **transverse diameter** in man, above and below, is 25 to 26 centimetres (9.7 to 10.1 inches), in females 23 to 24 centimetres (8.9 to 9.2 inches); above the nipple it is 1 centimetre more. The **antero-posterior diameter** (distance of anterior chest-wall from the tip of a spinous process) in the upper part of the chest is = 17 (6.6 inches), in the lower 19 centimetres (7.4 inches). Valentin found

that in a man, during the deepest inspiration, the chest on a level with the groove in the heart was increased about $\frac{1}{12}$ to $\frac{1}{7}$; while Sibson estimates the increase at the level of the nipple to be $\frac{1}{10}$.

Thoracometer.—In order to obtain a knowledge of the degree of movement—rising or falling—of the chest-wall during respiration, various instruments have been invented. The thoracometer (fig. 163) measures the elevation in different parts of the sternum. It consists of two metallic bars placed at right angles to each other; one of them, A, is placed on the vertebral column. On B there is placed a movable transverse bar, C, which carries on its free end a toothed rod, Z, directed downwards. The lower end of this rod is provided with a pad which rests on the sternum, while its toothed edge drives a small wheel, which moves an index, whose excursions are indicated on a circle with a scale attached to it.

The Cyrtometer of Woillez consists of a brass chain of movable links, to be applied in a definite direction to part of the chest-wall, *e.g.*, transversely on a level with the nipple, or vertically upon the mammillary or axillary lines anteriorly. There are freely movable links at two parts, which permit the chain to be easily removed, so that as a whole it still retains its form. The chain is laid upon a sheet of paper, and a line drawn with a pencil around its inner margin gives the form of the thorax (fig. 162). [Two thin bands of lead united by a leather hinge answers the same purpose.]

Anatomical Relations and Limits of the Lungs.—The extent and boundaries of the lungs are ascertained in the living subject by means of **percussion**, which consists in lightly tapping the chest-wall by means of a **percussion-hammer**. A

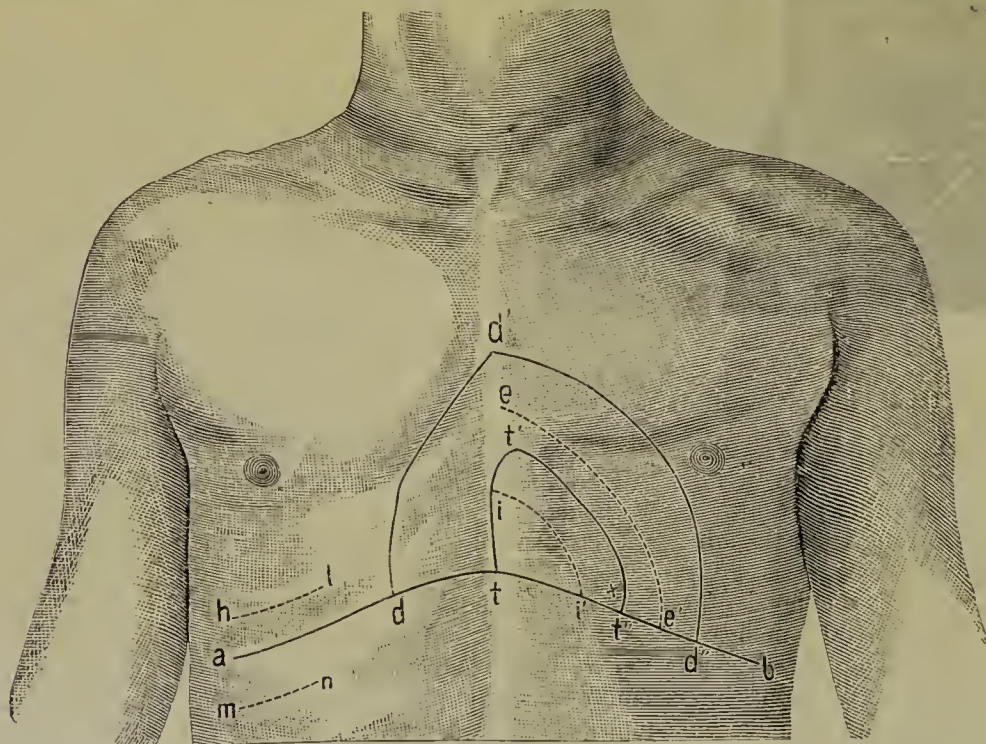


Fig. 164.

Topography of the lungs and heart. *h, l*, upward limit of margin of lung during deepest expiration; *m, n*, lower limit during deepest inspiration; *t, t', t''*, triangular area where the heart is uncovered by lung, dull percussion-sound; *d, d', d''*, muffled percussion-sound; *i, i'*, anterior margin of left lung reaches this line during deep inspiration, and during deep expiration it recedes as far as *e, e'*.

small ivory or bone plate or **pleximeter**, held in the left hand, is laid on the chest, and the hammer is made to strike this plate, whereby a sound is emitted, which sound varies with the condition of the subjacent lung-tissue. Whenever the lung-substance in contact with the chest-wall contains air, a clear resonant tone or sound—such as is obtained by striking a vessel containing air, a clear percussion-

sound—is obtained. Where the lung does not contain air, a dull sound—like striking a limb—is obtained. If the parts containing air be very thin, or only partially filled with air, the sound is “muffled.”

Fig. 164 indicates the relation of the lungs to the anterior surface of the chest. The *apices of the lungs reach 3 to 7 centimetres (1.1 to 2.7 inches) above the clavicles anteriorly*, while posteriorly they reach as high as the level of the seventh spinous process. The *lower margin of the right lung* in the passive position (moderate expiration) of the chest, commences at the *right margin of the sternum* at the insertion of the sixth rib, runs under the right nipple, nearly parallel to the upper border of the sixth rib, and descends a little in the axillary line, to the upper margin of the seventh rib, or even to the eighth rib [and to the ninth rib in the scapular line]. On the *left side* (apart from the position of the heart), the lower limit reaches as far down anteriorly as the right. In fig. 164 the line *a, t, b* shows the lowest limit of the passive lungs. *Posteriorly* both lungs reach as far down as the tenth rib. During the *deepest inspiration*, the lungs descend anteriorly as far as between the sixth and seventh ribs, and posteriorly to the eleventh rib—whereby the diaphragm is separated from the thoracic wall (fig. 164). During the *deepest expiration*, the lower margins of the lungs are elevated almost as much as they descend during inspiration. In fig. 164, *m, n* indicates the margin of the right lung during deep inspiration; *h, l*, during deep expiration. [The part of the chest-wall covered by the costal pleura is considerably larger than the circumference of the lung. This is specially marked at the lower margin of the lung, and where the left lung is incised over the heart. In these regions, during expiration, the surfaces of the visceral and parietal pleuræ are in contact, but during inspiration they are separated, and allow the thin margins of the lung to be insinuated between them. This available space is called **complemental space**, or “disposable” or **reserve pleural space** by Luschka (fig. 62).]

It is important to observe the relation of the margin of the left lung to the heart. In fig. 164 a somewhat triangular space, reaching from the middle of the point of insertion of the fourth rib to the sixth rib on the left side of the sternum, is indicated. In the passive chest the anterior surface of the pericardium lies in contact with the inner surface of the thoracic wall in this triangular area (§ 56). This area is represented by the triangle, *t, t', t''*, and percussion over it gives a dull sound (**superficial cardiac dulness**, p. 88).

In the area of the larger triangle, *d, d', d''*, where the heart is separated from the chest-wall by the thin anterior margins of the lung, percussion gives a muffled sound, while further outwards a clear lung percussion-sound is obtained. During deep inspiration, the inner margin of the left lung reaches over the heart as far as the insertion of the mediastinum, whereby the dull sound is limited to the smallest triangle, *t, i, i'*. Conversely, during very complete expiration, the margin of the lung recedes so far that the cardiac dulness embraces the space, *t, e, e'*.

[The right lung consists of three lobes, and the left of two. The relations of these lobes to the chest-wall are important clinically, and may be tabulated as follows, according to Gibson and Russell :—

Right Lung (3 lobes).

	Anteriorly (Mammary line).	Laterally.	Posteriorly.
<i>Upper lobe,</i>	From apex to 4th or 5th rib.	To 4th rib.	From apex to spine of scapula.
<i>Middle lobe,</i>	From 4th or 5th rib to inferior margin of lung.	From 4th to 6th rib.	<i>Nil.</i>
<i>Lower lobe,</i>	<i>Nil.</i>	From 6th to 8th rib.	From spine of scapula to 10th rib.

Left Lung (2 lobes).

	Anteriorly (Mammary line.)	Laterally.	Posteriorly.
Upper lobe,	From apex to 6th rib.	To 4th rib.	From apex to spine of scapula.
Lower lobe,	<i>Nil.</i>	From 4th rib to base.	From spine of scapula to base.

115. PATHOLOGICAL PERCUSSION-SOUNDS.—**Abnormal Dulness.**—The normal clear resonant percussion-sound of the lungs becomes muffled when infiltration takes place into the lungs, so as to diminish the normal amount of air within them, or when the lungs are compressed from without, *e.g.*, by effusion of fluid into the pleura. The percussion-sound becomes clearer when the chest-wall is very thin, as in spare individuals, during very deep inspiration, and especially in emphysema, where the air-vesicles of certain parts of the lung (apices and margins) become greatly dilated.

The **pitch** of the percussion-sound ought also to be noted. It depends upon the greater or less tension of the elastic pulmonary tissue, and on the elasticity of the thoracic wall. The tension of the elastic tissue is increased during inspiration and diminished during expiration, so that even under physiological conditions the pitch of the sound varies.

The sound is said to be **tympanitic** when it has a musical quality resembling in its timbre the sound produced on drums, and when it has a slight variation in pitch. If a caoutchouc ball be placed near the ear, on tapping it gently, a well-marked tympanitic sound is heard, and the sound is of higher pitch the smaller the diameter of the ball. A tympanitic sound is always produced on tapping the trachea in the neck. *A tympanitic sound produced over the chest is always indicative of a diseased condition.* It occurs in cases of cavities or vomicæ within the substance of the lung (the sound becomes deeper when the mouth, or better, the mouth and nose, are closed), when air is present in one pleural cavity, as well as in conditions where the tension of the pulmonary tissues is diminished. The tympanitic sound resembles the *metallic tinkling* which is heard in large pathological cavities in the lungs, or which occurs when the pleural cavity contains air, and when the conditions which permit a more uniform reflection of the sound-waves within the cavity are present.

[When a cavity, freely communicating with a large bronchus, exists in the upper and anterior part of the lung, a peculiar “**cracked-pot sound**” is heard on percussing over the part. Some notion of this sound may be obtained by clasping the two hands so as to bring the palms nearly together, leaving an air-space between, and then striking them on the knee. When percussion is made over a large cavity communicating with a bronchus, some of the air is expelled, and the sound thereby emitted is blended with the fundamental note of the air in the cavity itself, the combination of these two sounds thus producing the “cracked-pot” sound.]

Resistance.—When percussing a chest, we may determine whether the substance lying under the portion of the chest under examination presents great or small resistance to the blow, either of the percussion-hammer or of the tips of the fingers, as the case may be, [*e.g.*, in great pleuritic effusion exerting much pressure on, and so distending, the thoracic walls.]

Phonometry.—If the stem of a vibrating tuning-fork be placed on the chest-wall over a part containing air, its sound is intensified; but if it be placed over a portion of the lung which contains little or no air, its sound is enfeebled (*von Baas*).

116. THE NORMAL RESPIRATORY SOUNDS.—If the ear directly, or through the medium of a **stethoscope**, be placed in connection with the chest-wall, we hear over the entire area, where the lung is in contact with the chest, the so-called “**normal vesicular sound**,” which is audible *during inspiration*, and its typical characters may be studied by listening in the infra-scapular region in an adult. It is a fine, soft, sighing or breezy sound, [which gradually increases in intensity until it reaches a maximum, and falls away before expiration begins]. It is said to be caused by the sudden dilatation of the air-vesicles (hence “**vesicular**”) during inspiration, and it is also ascribed to the friction of the current of air entering the alveoli. The sound has, at one time, a soft, at another, a sharper character; the latter occurs constantly in children up to 12 years of age. In their case, the sound is sharper, because the air, in entering vesicles one-third narrower, is subjected to greater friction. This is followed by an *expiratory* sound, which

may be absent during quiet breathing. It is a feeble sighing sound, of an indistinct soft character, caused by the air passing out of the air-vesicles, is three or four times shorter than the inspiratory, is loudest at first, and soon disappears, the latter part of the expiratory act giving rise to no audible sound. Its absence is not a sign of disease, but when it is prolonged and loud, suspicion is aroused. The relative duration of the respiratory sounds is—

Inspiratory sound : Expiratory sound : : 3 : 1.

Bronchial Respiration.—Within the larger air-passages—larynx, trachea, bronchi—during inspiration and expiration, there are loud, rough, harsh sounds like a sharp *h* or *ch*—the “*bronchial*”—the laryngeal, tracheal, or “*tubular*” sound, or breathing. [In normal bronchial breathing, as heard over the trachea, there is a pause between the inspiratory and expiratory sounds, which are of nearly equal duration and of about the same intensity throughout. These sounds are also heard between the scapulæ, at the level of the fourth dorsal vertebra (bifurcation of trachea), and they occur also during expiration, being slightly louder on the right side, owing to the slightly greater calibre of the right bronchus. At all other parts of the chest, the vesicular sound obscures the tubular or bronchial sound. If the air-vesicles are deprived of their air, the tubular breathing becomes distinct.]

Bronchial respiration is produced chiefly in the larynx, owing to the formation of air-eddies in consequence of the narrowing of the respiratory part of the glottis. This “laryngeal stenosis sound” excites resonance of the tracheo-bronchial column of air, and communicates to it the specific character of bronchial breathing which is heard over the large tubes of the bronchial system (*Dehio*).

[On listening with a stethoscope over the trachea, or better still, over the cervical vertebræ, the sounds heard vary according as the mouth is open or closed. *With the mouth open*, the soft-blowing respiratory sounds are about of equal duration, are separated by a short pause, but the expiratory is louder than the inspiratory. *If the mouth be closed*, and respiration consequently carried on through the nose, it is found that the sounds become harsher and louder. The character of the sounds also vary with the rapidity of breathing.]

It is asserted that, when lungs containing air are placed over the trachea, the tubular sound there produced becomes vesicular. In this case, we must suppose that the vesicular sound arises from the tubular breathing becoming weakened, and acoustically altered by being conducted through the lung alveoli. A sighing sound is often produced at the apertures of the nose and mouth during forced inspiration.

117. PATHOLOGICAL RESPIRATORY SOUNDS.—[The breath-sounds heard in disease may be merely modifications of the normal vesicular or bronchial sounds, or new sounds, such as friction sounds, râles, or rhonchi.]

[**Puerile Breathing** is merely an exaggerated vesicular sound, so called because it resembles the louder vesicular sound heard in children. It occurs when some part of the lung is unable to act, and there is, as it were, extra work of the other parts to compensate, and thus the sound is exaggerated.]

(1) **Bronchial or Tubular Breathing** occurs over the entire area of the lung, either when the air-vesicles are *devoid of air*, which may be caused by the exudation of fluid or solid constituents, or when the lungs are compressed from without. In both cases vesicular sounds disappear, and the condensed or solidified lung-tissue *conducts* the tubular sound of the large bronchi to the surface of the chest. [The sound heard over a hepatised lobe of the lung in pneumonia is a typical example.] It also occurs in large cavities, with resistant walls near the surface of the lung, provided these cavities communicate with a large bronchus. [In this case it is termed **cavernous breathing**.]

(2) The **amphoric sound** is compared to that produced by blowing over the mouth of an empty bottle. [It occurs either when a *cavity*—at least the size of the fist—exists in the lung, which is so blown into during respiration that a peculiar amphoric-like sound, with a metallic timbre, called **metallic tinkling**, is produced; or when the lung still contains air, and is capable of expansion; as there is still air in the pleural cavity, it acts as a resonator, and causes an amphoric sound, simultaneous with the change of air in the lungs. [The amphoric sound or echo and metallic tinkling are the only certain signs of the existence of a cavity in the lung.]]

(3) If **obstruction** occurs in the course of the air-passages of the lungs, various results may accrue, according to the nature of the resistance:—(a) owing to various causes, *e.g.*, in the

apices of the lungs, there may be partial swelling of the walls of the air-tubes, or infiltration into the air-cells which hinders the regular supply of air. In these cases, parts of the lung are not supplied with air continuously; it only reaches them periodically, when a **cogwheel sound** occurs. A similar sound may be heard occasionally in a normal lung; when the muscles of the chest contract in a periodic spasmodic manner. (b) When the air entering large bronchi causes the formation of bubbles in the mucus which may have accumulated there, "**mucous râles**" are produced. They also occur in small spaces when the walls are separated from their fluid contents by the air entering during inspiration, or when the walls, being adherent to each other, are suddenly pulled asunder. The râles are distinguished as *moist* (when the contents are fluid), or as *dry* (when the contents are sticky); they may be inspiratory, expiratory, or continuous, or they may be coarse or fine; further, there is the very fine crepitation, or crackling sound, and, lastly, the metallic tinkling caused in large cavities through resonance. [Crepitation or vesicular râles are fine crepitating sounds like those produced by rubbing a lock of hair between the fingers near one's ear, or the sounds produced when salt is thrown on a fire; they occur only during inspiration, and are a proof that some air is entering the air-vesicles. It is heard in its typical form during the first stage of pneumonia, and seems to be produced by the bursting of minute bubbles of air in a fluid.] (c) When the mucous membrane of the bronchi is greatly swollen, or is so covered with viscid mucus that the air must force its way through, deep sonorous **rhonchi** (*rhonchi sonori*) may occur in the large air-passages, and clear shrill sibilant sounds (*rhonchi sibilantes*) in the smaller ones. [Rhonchi are whistling sonorous sounds, with a squeaking character, and are usually due to catarrh or to affections of the bronchial mucous membrane or bronchitis. When they are of low pitch, and produced in the large bronchial tubes, they are spoken of as **sonorous rhonchi**, but when they are of high pitch, and reproduced in the small bronchial tubes, they are **sibilant rhonchi**.] When there is extensive bronchial catarrh, not unfrequently we feel the chest-wall vibrating with the râle sounds (**bronchial fremitus**).

(4) If fluid and air occur together in one pleural cavity in which the lung is collapsed, on shaking the person's thorax vigorously we hear a sound such as is produced when air and water are shaken together in a bottle. This is the **succussion sound** of Hippocrates. Much more rarely this sound is heard under similar conditions in large pulmonary cavities.

(5) **Pleural Friction**.—When the two opposed surfaces of the pleura are inflamed, have become soft, and are covered with exudation, they move over each other during respiration, and in doing so give rise to **friction sounds**, which can be felt (often by the patient himself), and can also be heard. The sound is comparable to the sound produced by bending new leather.

(6) **Pectoral Fremitus**.—When we speak or sing in a loud tone, the walls of the chest vibrate, because the vibration of the vocal cords is propagated throughout the entire bronchial ramifications. The vibration is, of course, greatest near the trachea and large bronchi. The ear cannot detect the sounds distinctly. If there be much exudation or air in the pleura, or great accumulation of mucus in the bronchi, the pectoral fremitus is diminished or altogether absent. [In health, when a person speaks, the **vocal resonance** over the trachea, although loud, may be inarticulate; and on listening over the sternum the sound is diminished and quite inarticulate; while over the chest-wall generally the sound, though distinct, is feeble.]

All conditions which cause bronchial breathing increase the pectoral fremitus. Under normal circumstances, therefore, it is louder where bronchial breathing is heard normally. The ear hears an intensified sound, called **bronchophony**, [which is a sound like that heard normally over the trachea or bronchi, but audible over the vesicular lung-tissue. The conditions that cause it are the same as those on which bronchial breathing depends, so that it is heard in pneumonia and phthisis. If, through effusion into the pleura or inflammatory processes in the lung-tissue, the bronchi are pressed flat, a peculiar bleating sound (**ægophony**) may be heard.]

118. PRESSURE IN THE AIR-PASSAGES DURING RESPIRATION.—

Respiratory Pressure.—If a manometer be tied into the trachea of an animal, so that the respiration goes on completely undisturbed, *i.e.*, **normal respiration**, during every inspiration there is a negative pressure (-3 mm. Hg) and during expiration a positive pressure. Donders placed the U-shaped manometer tube in one nostril, closed his mouth, leaving the other nostril open, and respired quietly. During every quiet inspiration the mercury showed a negative pressure of -1 mm., and during expiration a positive pressure of $2-3$ mm. (Hg).

Forced Respiration.—As soon as the air was inspired or expired with greater force, the variations in pressure became very much greater, *e.g.*, during speaking, singing, and coughing. The inspiratory pressure was $= 57$ mm. ($36-74$), the greatest expiratory pressure $+ 87$ ($82-100$) mm. Hg. The pressure of forced expiration, therefore, is 30 mm. greater than the inspiratory pressure (*Donders*).

Resistance to Inspiration.—Notwithstanding this, we must not conclude that the expiratory muscles act more powerfully than the inspiratory; for during inspiration a variety of resistances have to be overcome, so that after these have been met, there is only a residue of the force for the aspiration of the mercury. The resistances to be overcome by the inspiratory muscles are:—(1) The *elastic tension of the lungs*, which during the deepest expirations = 6 mm.; during the deepest inspirations = 30 mm. Hg (§ 107). (2) The raising of the weight of the chest. (3) The *elastic torsion* of the costal cartilages. (4) The depression of the abdominal contents, and the elastic distention of the abdominal walls. All these not inconsiderable resistances, which the inspiratory muscles have to overcome, act during expiration, and aid the expiratory muscles. The forces concerned in inspiration are decidedly much greater than those of expiration.

Intra-thoracic Pressure.—As the lungs within the chest, in virtue of their elasticity, continually strive to collapse, necessarily they must cause a negative pressure *within the chest*. This amounts in dogs, during inspiration, to -7.1 to -7.5 mm. Hg, and during expiration to -4 mm. Hg. The corresponding values for man have been estimated at -4.5 mm. Hg and -3 mm. Hg, by Hutchinson.

[We must distinguish between the **respiratory pressure** of the air *within the respiratory passages*, and the **intra-thoracic pressure**. The former is the same as the atmospheric pressure when the chest is passive, but less than it as the chest is being enlarged, and greater than it when it is being diminished in size. The **intra-thoracic pressure** is the pressure within the chest, but *outside the lungs*, i.e., in the pleura, mediastinum, &c. It is negative, i.e., less than the atmospheric pressure, and must vary with the degree of distention of the lungs.]

Methods of Estimating Intra-Thoracic Pressure.—A direct estimation was made by Adamkiewicz and Jacobson. A trocar with its stylette was forced into the fourth left intercostal space near the sternum and pushed into the pericardium (sheep). The stylette was then withdrawn, and the trocar connected with a manometer, and the negative pressure of -3 to -5 mm. Hg was obtained. During severe dyspnoea it was -9 mm. Hg. Rosenthal introduced an **œsophageal sound** with an elastic ampulla on its lower end into the œsophagus, so that the ampulla came to lie opposite the posterior mediastinum. The sound was connected with a registering tambour or manometer. During inspiration the manometer fell, and during expiration it rose.]

Even the greatest inspiratory or expiratory pressure is always much less than the blood-pressure in the large arteries; but if the pressure be calculated upon the entire respiratory surface of the thorax, very considerable results are obtained.

Pneumatometer.—This instrument of Waldenburg is merely a mercurial manometer fixed to a stand, and connected to an elastic tube with a suitable mouthpiece, which is fitted over the mouth and nose, while the variations of the Hg can be read off on a scale. [In the male, the expiratory pressure is 90–120 mm. Hg, and the inspiratory 70–100. The relation of the pressures during expiration and inspiration is more important than the absolute pressure.] The inspiratory pressure is diminished in nearly all diseases where the expansion of the lung is impaired [phthisis]; or the expiratory pressure is diminished, as in emphysema and asthma.

[The Lungs before birth] are in an **atelectatic condition**, i.e., they contain no air. The alveoli are lined by cubical, nucleated granular cells, and their surfaces are in apposition, so that there are no alveolar cavities; similarly the walls of the bronchioles are in contact, while the cavity which exists in the larger bronchi and trachea contains fluid. At the first breath the air sucked in has to overcome the adhesion of the surfaces of the bronchi and alveolar epithelium, and as inspiration follows inspiration, gradually the respiratory passages are opened up. It takes some time to establish a fully distended condition of the lung. In a newly-born animal there is no negative pressure in the pleural cavity, for the lungs have not yet been distended, nor do the lungs collapse when the chest is opened. It is only when the elastic tension of the lungs is brought into play by the chest being distended, that the negative pressure obtains within the pleural cavity, and the lungs collapse when the chest is opened. The distention of the lungs takes place gradually, and seems to be brought about by the chest growing more rapidly than the lungs within it; so that even in the phase of expiration the lungs are kept distended.]

Effects of the first Respiration on the Thorax.—Until birth the airless lungs are completely collapsed (atelectatic) within the chest, and fill it, so that on opening the chest in a dead foetus, pneumo-thorax does not occur (*Bernstein*). Supposing, however, respiration to have been fully established after birth, and air to have freely entered the lungs, if a manometer be placed in connection with the trachea, and the chest be opened, the manometer will register a pressure of 6 mm. Hg, due to the collapse of the elastic lungs. Bernstein supposes that the thorax assumes a new permanent form, due to the first respiratory distention; it is as if, owing to the respiratory elevation of the ribs, the thorax had become permanently too large for the lungs, which are, therefore, kept permanently distended, but collapse as soon as air passes into the pleura. When a lung has once been filled with air, it cannot be emptied by pressure from without, as the small bronchi are compressed before the air can pass out of the alveoli. The expiratory muscles cannot possibly expel all the air from the lungs, while the inspiratory muscular force is sufficient to distend the lungs beyond their elastic equilibrium. Inspiration distends the lungs, increasing their elastic tension, while expiration diminishes the tension without abolishing it.

119. APPENDIX TO RESPIRATION.—Nasal Breathing.—During quiet respiration we usually breathe—or ought to breathe—through the nostrils, the mouth being closed. The current of air passes through the pharyngo-nasal cavity—so that, in its course during inspiration, it is (1) *warmed* and rendered *moist*, and thus irritation of the mucous membrane of the air-passages by the cold air is prevented; (2) small *particles of soot*, or other foreign substances in the air, adhere to, and become embedded in the mucus covering the somewhat tortuous walls of the respiratory passages, and are carried outwards by the agency of the ciliated epithelium of the respiratory passages; (3) disagreeable odours and certain impurities are detected by the sense of smell.

If a lung be inflated, air constantly passes through the walls of the alveoli and trachea. This also occurs during violent expiratory efforts (cutaneous emphysema in whooping-cough), so that pneumo-thorax may occur (*J. R. Ewald and Kobert*).

Pulmonary Œdema, or the exudation of lymph into the pulmonary alveoli, occurs—(1) When there is very great resistance to the blood-stream in the aorta or its branches, *e.g.*, by ligaturing all the arteries going to the head, or the arch of the aorta, so that only one carotid remains pervious. (2) When the pulmonary veins are occluded. (3) When the left ventricle, owing to mechanical injury, ceases to beat, while the right ventricle goes on contracting (§ 47). These conditions produce at the same time anæmia of the vaso-motor centre, which results in stimulation of that centre, and consequent contraction of all the small arteries. Thus the blood-stream through the veins to the right heart is favoured, and this in its turn favours the production of œdema of the lungs. [The injection of muscarin rapidly causes pulmonary œdema, due to the increase of pressure and slowing of the blood-stream in the pulmonary capillaries. It is set aside by atropin (*Weinzeig, Grossmann*).]

120. MODIFIED RESPIRATORY MOVEMENTS.—(1) **Coughing** consists in a sudden violent expiratory explosion after a previous deep inspiration and closure of the glottis, whereby the glottis is forced open, and any substance, fluid, gaseous, or solid, in contact with the respiratory mucous membrane is violently ejected through the open mouth. It is produced voluntarily or reflexly; in the latter case, it can be controlled by the will only to a limited extent.

[**Causes.**—A cough may be discharged **reflexly** from a large number of surfaces (fig. 165):—(1) A draught of cold air striking the *skin*, especially of the upper part of the body. This may cause congestion of blood in the air-passages, this in turn exciting the cough. (2) More frequently it is discharged from the respiratory mucous membrane, especially of the larynx, the sensory branches of the vagus and the superior laryngeal nerve being the afferent nerves. A cough cannot be discharged from every part of the larynx: thus there is none from the true vocal cords, but only from the glottis respiratoria. All other parts of the larynx are inactive, and so is the trachea as far as the bifurcation, where stimulation excites a cough (*Kohts*). (3) Sometimes an offending body, such as a pea or inspissated cerumen in the external auditory meatus, gives rise to coughing, the afferent nerve being the auricular branch of the vagus. (4) There seems to be no doubt that there may be a “*gastric or stomach cough*” produced by stimulation of the gastric branches of the vagus, especially in cases of indigestion, accompanied by irritation of the larynx and trachea. (5) Irritation of the costal pleura and even of the œsophagus (*Kohts*). (6) Irritation of some parts of the nose. (7) Sometimes also from irritation of the pharynx, as by an elongated uvula. (8) In some diseases of the liver, spleen, and generative organs, when pressure is exerted on these parts.]

(2) **Hawking**, or clearing the throat.—An expiratory current is forced in a continuous stream through the narrow space between the root of the tongue and the depressed soft palate, in order to assist in the removal of foreign bodies. When the act is carried out periodically, the closed glottis is suddenly forced open, and it is comparable to a voluntary gentle cough. This act can only be produced voluntarily.

(3) **Sneezing** consists in a sudden violent expiratory blast through the *nose*, for the removal of mucus or foreign bodies (the mouth being rarely open) after a simple or repeated spasm-like inspiration—the glottis remaining open. It is usually caused reflexly by stimulation of sensory nerve-fibres of the nose [nasal branch of the fifth nerve], or by sudden exposure to a bright light [the afferent nerve is the optic]. This reflex act may be interfered with to a certain extent, or even prevented, by stimulation of sensory nerves; or firmly compressing the nose where the nasal nerve issues. The continued use of sternutatories, as in persons who take snuff, dulls the sensory nerves, so that they no longer act when stimulated reflexly.

[**Sternutatories or Errhines**, such as powdered ipecacuanha, snuff, and euphorbium, also increase the secretion from the nasal glands. The afferent impulses sent to the respiratory centre also affect the vaso-motor centre, so that, even when sneezing does not occur, the blood-pressure throughout the body is raised.]

(4) **Snoring** occurs during respiration through the open mouth, whereby the inspiratory and expiratory stream of air throws the uvula and soft palate into vibration. It is involuntary, and usually occurs during sleep, but it may be produced voluntarily.

(5) **Gargling** consists in the slow passage of the expiratory air-current in the form of bubbles through a fluid lying between the tongue and the soft palate, when the head is held backwards. It is a voluntary act.

(6) **Crying**, caused by emotional conditions, consists in short, deep inspirations, long expirations with the glottis narrowed, relaxed facial and jaw muscles, secretion of tears, often combined with plaintive inarticulate expressions. When crying is long continued, sudden and spasmodic involuntary contractions of the diaphragm occur, which cause the inspiratory sounds in the pharynx and larynx known as sobbing. This is an involuntary act.

(7) **Sighing** is a prolonged inspiration, usually combined with a plaintive sound, often caused involuntarily, owing to painful or unpleasant recollections.

(8) **Laughing** is due to short rapid expiratory blasts through the rima glottidis, which cause a clear tone, and there are characteristic inarticulate sounds in the larynx, with vibrations of the soft palate. The mouth is usually open, and the countenance has a characteristic expression, owing to the action of the *M. zygomaticus major*. It is usually involuntary, and can only be suppressed, to a certain degree, by the will (by forcibly closing the mouth and stopping respiration).

(9) **Yawning** is a prolonged deep inspiration occurring after successive attempts at numerous inspirations—the mouth, fauces, and glottis being wide open; expiration shorter—both acts often accompanied by prolonged characteristic sounds. It is quite involuntary, and is usually excited by drowsiness or ennui.

[(10) **Hiccough** is due to a spasmodic involuntary contraction of the diaphragm, causing an inspiration, which is arrested by the sudden closure of the glottis, so that a characteristic sound is emitted. Not unfrequently it is due to irritation of the gastric mucous membrane, and sometimes it is a very troublesome symptom in uræmic poisoning.]

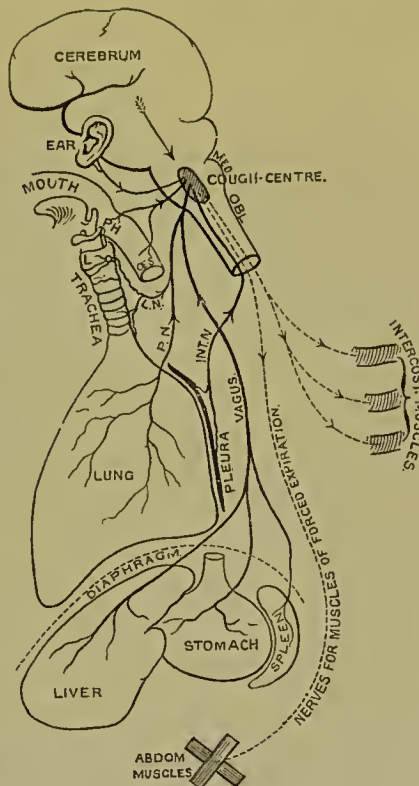


Fig 165.

Scheme of the afferent nerves through which coughing may be excited reflexly. The efferent nerves are dotted.

121. CHEMISTRY OF RESPIRATION—CARBON DIOXIDE, OXYGEN, and WATERY VAPOUR GIVEN OFF.—I. Estimation of CO_2 .—1. The volume of CO_2 is estimated by means of the anthracometer (fig. 166, II). The volume of gas is collected in a graduated tube, *rr*, provided with a bulb at one end (previously filled with water and carefully calibrated, *i.e.*, the exact amount which each part of the tube contains is accurately measured), and the tube is closed. The lower end has a stop-cock, *h*, and to this is screwed a flask, *n*, completely filled

with a solution of caustic potash; the stop-cock is then opened, the potash solution is allowed to ascend into the tube, which is moved about until all the CO_2 unites with the potash to form potassium carbonate. Hold the tube vertically and allow the potash to run back into the flask, close the stop-cock, and remove the bottle with the potash. Place the stop-cock under water, open it, and allow the water to ascend in the tube, when the space in the tube occupied by the fluid indicates the volume of CO_2 which is combined with the potash.

2. **By Weight.**—A large quantity of the mixture of gases which has to be investigated is made to pass through a Liebig's bulb filled with caustic potash. The potash apparatus having been carefully weighed beforehand, the increase of weight indicates the amount of CO_2 which has been taken up by the potash from the air passed through it.

3. **By Titration.**—A large volume of the air to be investigated is conducted through a known volume of a solution of barium hydrate. The CO_2 unites with the barium and forms barium carbonate. The fluid is neutralised with a standard solution of oxalic acid, and the more barium that has united with the CO_2 the smaller will be the amount of oxalic acid used, and *vice versa*.

II. **Estimation of Oxygen.**—According to volume—(a) By the union of the O with potassium pyrogallate. The same procedure is adopted as for the estimation of CO_2 , only the flask, *n*,

is filled with the pyrogallate solution instead of potash. (b) By explosion in an eudiometer (*Blood gases*, § 35).

III. **Estimation of Watery Vapour.**—The air to be investigated is passed through a bulb containing concentrated sulphuric acid, or through a tube filled with pieces of calcium chloride. The amount of water is directly indicated by the increase of weight.

122. **METHODS OF INVESTIGATION.**—Collecting the Expired Air.—(1) The air expired may be collected in the cylinder of the spirometer, which is suspended in concentrated salt solution to avoid the absorption of CO_2 (§ 108).

Andral and Gavarret's Apparatus.—The operator breathed

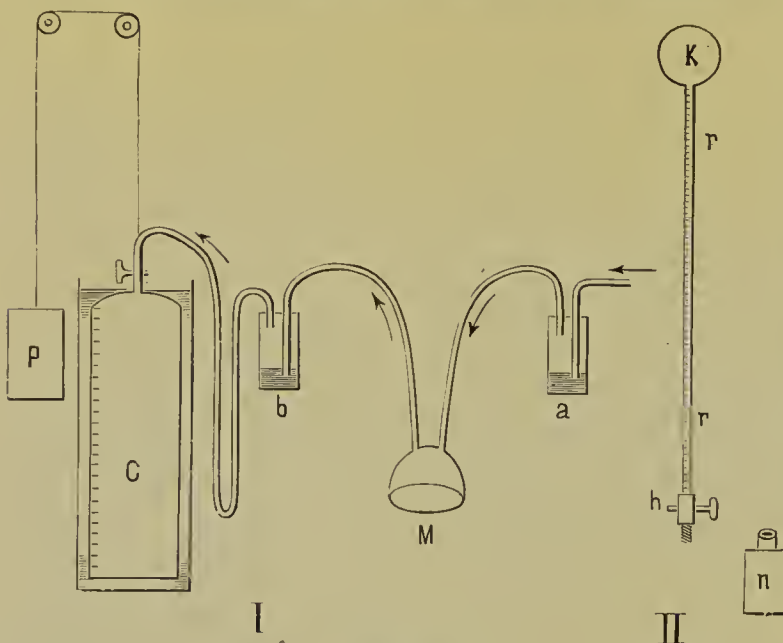


Fig. 166.

I. Apparatus of Andral and Gavarret for collecting the expired air. C, large cylinder to collect the air expired; P, weight to balance cylinder; *a*, *b*, two Müller's valves; M, mouthpiece. II. Anthracometer of Vierordt.

several times into a capacious cylinder (fig. 166). A mouthpiece (M) was placed air-tight over the mouth while the nostrils were closed. The direction of the respiratory current was regulated by two "Müller's Valves" (mercurial), (*a* and *b*). With every inspiration the bottle or valve *a* (filled below with Hg, and hermetically closed above) permits the air inspired to pass to the lungs—during every expiration the expired air can pass only through *b* to the collecting-cylinder C.

(2) If the gases given off by the skin are to be collected, a limb, or whatever part is to be investigated, is secured in a closed vessel, and the gases so obtained are analysed.

II. The most important apparatus for this purpose are those of—(a) **Scharling**, which consists of a closed box, A, of sufficient size to contain a man (fig. 167). It is provided with an inlet *z* and outlet *b*. The latter is connected with an aspirator, C, a large barrel filled with water. When the stop-cock, *h*, is opened and the water flows out of the barrel, fresh air will rush in continuously into the box, A, and the air mixed with the expired gases will be drawn towards C. A Liebig's bulb, *d*, filled with caustic potash, is connected with the entrance tube, *z*, through which the ingoing air must pass, whereby it is completely deprived of CO_2 , so that the person experimented on is supplied with air free from CO_2 . The air passing out by the exit tube, *b*, has to pass first through *e*, where it gives up its watery vapour to sulphuric acid,

whereby the amount of watery vapour is estimated by the increase of the weight of the apparatus, *e*. Afterwards the air passes through a bulb, *f*, containing caustic potash, which absorbs all the CO₂, while the tube, *g*, filled with sulphuric acid, absorbs any watery vapour.

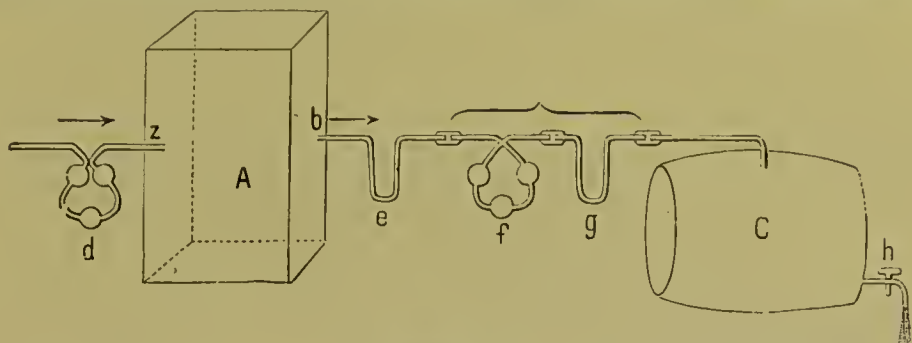


Fig. 167.

Scharling's apparatus. *d*, bulb containing caustic potash to absorb CO_2 from ingoing air; *A*, box for animal experimented on; *e* and *g*, tubes containing sulphuric acid to absorb watery vapour; *f*, potash bulb to absorb CO_2 given off; *C*, vessel filled with water to aspirate air; *h*, stop-cock.

that may come from f . The increase in weight of f and g indicates the amount of CO_2 . The total volume of air used is known from the capacity of C.

(b) **Regnault and Reiset's Apparatus** is more complicated, and is used when it is necessary to keep animals for some time under observation in a bell-jar. It consists of a globe, R, in which is placed the dog to be experimented on (fig. 168). Around this is placed a cylinder, g, g (provided with a thermometer, *t*), which may be used for calorimetric experiments. A

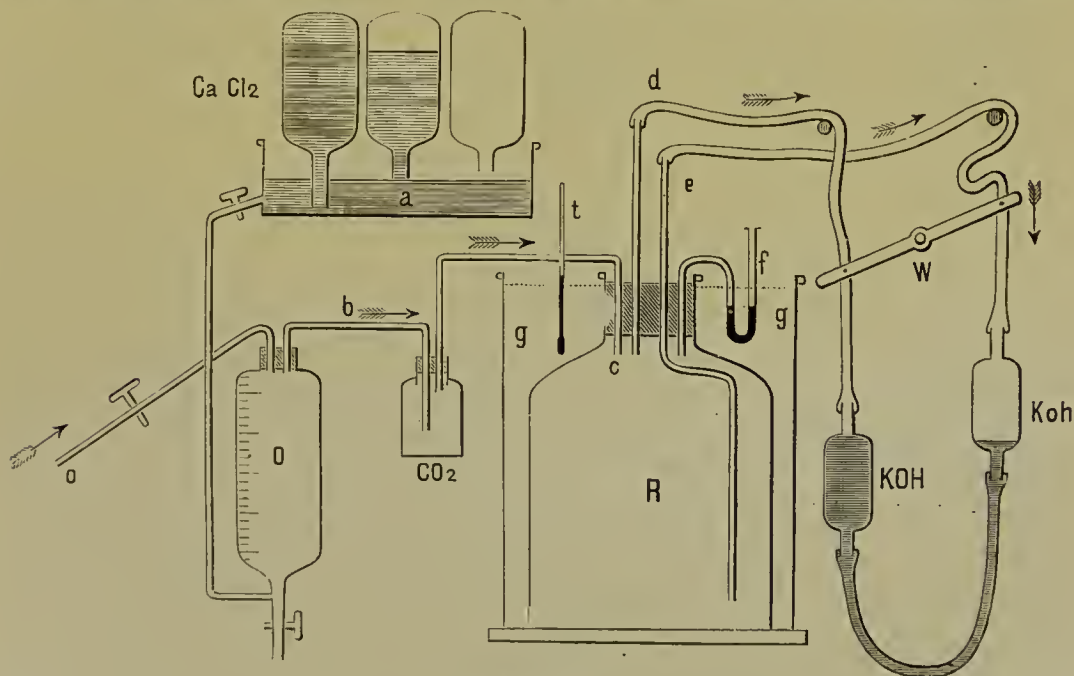


fig. 168.

Scheme of the respiration apparatus of Regnault and Reiset. R, globe for animal; *g, g*, outer casing for R, provided with a thermometer, *t*; *d* and *e*, exit tubes to movable potash bulbs KOH and *Koh*; O, ingoing oxygen; CO₂, vessel to absorb any carbonic acid; CaCl₂, apparatus for estimating the amount of O supplied; *f*, manometer.

tube, *c*, leads into the globe, R; through this tube passes a known quantity of pure oxygen (fig. 168, O). To absorb any trace of CO₂, a vessel containing potash (fig. 168, CO₂) is placed in the course of the tube. The vessel for measuring the O is emptied towards R, through a solution of calcium chloride from a large pan (CaCl₂) provided with large flasks. Two tubes,

2. **Aqueous vapour** is always present in the air, but it varies greatly in amount, and generally increases with the increase of the temperature of the air. We distinguish (a) the *absolute moisture*, i.e., the quantity of watery vapour which a volume of air contains in the form of vapour; and (b) the *relative moisture*, i.e., the amount of watery vapour which a volume of air contains with respect to its temperature.

Experience shows that people generally can breathe most comfortably in an atmosphere which is not completely saturated with aqueous vapour according to its temperature, but is only saturated to the extent of 70 per cent. If the air be too dry, it irritates the respiratory mucous membrane; if too moist, there is a disagreeable sensation; and if it be too warm, a feeling of closeness. Hence, it is important to see that the proper amount of watery vapour is present in the air of our sitting-rooms, bedrooms, and hospital wards.

The **absolute amount** of moisture varies:—In towns during the day it increases with increase of temperature, and diminishes when the temperature falls; it also varies with the direction of the wind, season of the year, and the height above sea-level.

The **relative amount** of moisture is greatest at sunrise, least at midday; small on high mountains; greater in winter than in summer; larger with a south or a west wind than with a north or an east wind.

The air in midsummer contains absolutely three times as much watery vapour as in mid-winter, nevertheless the air in summer is *relatively* drier than the air in winter.

3. The air **expands by heat**. Rudberg found that 1000 volumes of air, at 0°, expanded to 1365 when heated to 100° C.

4. The **density** of the air diminishes with increase of the height above the sea-level.

124. COMPOSITION OF EXPIRED AIR.—1. The expired air contains **more CO₂**—in normal respiration = 4.38 vols. per cent. (3.3 to 5.5 per cent.), so that it contains nearly 100 times more CO₂ than the atmospheric air.

2. It contains **less O** (4.782 vols. per cent. less) than the atmospheric air, i.e., it contains only 16.033 vols. per cent. of O.

3. **Respiratory Quotient.**—Hence, during respiration, more O is taken into the body from the air than CO₂ is given off; so that the volume of the expired air is ($\frac{1}{10}$ to $\frac{1}{50}$) smaller than the volume of the air inspired, both being calculated as dry, at the same temperature, and at the same barometric pressure. The relation of the O absorbed to the CO₂ given off is 4.38 : 4.782. This is expressed by the “**respiratory quotient**”—

$$\frac{\text{CO}_2}{\text{O}} \left(= \frac{4.38}{4.782} \right) = 0.916.$$

4. An excessively small quantity of **N** is added to the expired air (*Regnault and Reiset*). Segen found that all the N taken in with the food did not reappear in the excreta (urine and fæces), and he assumed that a small part of it was given off by the lungs.

5. During ordinary respiration the expired air is **saturated with watery vapour**. It is evident, therefore, that when the watery vapour in the air varies, the lungs give off different quantities of water from the body. The percentage of watery vapour falls during rapid respiration (*Moleschott*).

6. The expired air is **warmer** (36°·3 C.). It is very near the temperature of the body, and although the temperature of the surrounding atmosphere be very variable, the temperature of the expired air still remains nearly the same.

Fig. 170 shows the instrument used by Valentin and Brunner to determine the temperature of the expired air. It consists of a glass tube, A, A, with a mouthpiece, B, and in it is a fine

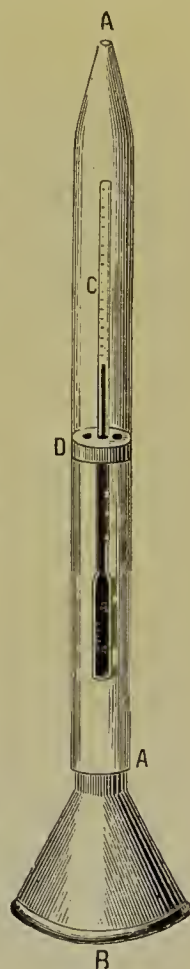


Fig. 170.

thermometer, C. The operator breathes through the nose and expires slowly through the mouthpiece into the tube.

Temperature of the Air.	Temperature of the Expired Air.
-6.3° C.,	+29.8° C.
+17-19° C.,	+36.2-37° C.
+44° C.,	+38.5° C.

7. The **diminution of the volume** of the expired air mentioned under (3) is far more than compensated by the warming which the inspired air undergoes in the respiratory passages, so that the volume of the expired air is one-ninth greater than the air inspired.

8. A very small quantity of **ammonia** is found in the expired air = 0.0204 grams in 24 hours; it is probably derived from the blood.

9. Small quantities of **H** and **CH₄** are expired, both being absorbed from the intestine. In herbivora, Reiset found that 30 litres of CH₄ were expired in 24 hours.

[The toxicity of the exhalations from the lungs of animals described by Brown-Séguard has not been confirmed by other observers.]

125. DAILY QUANTITY OF GASES EXCHANGED.—As under normal circumstances more O is absorbed than there is CO₂ given off (equal volumes of O and CO₂ contain equal quantities of O), a part of the O must be used for other oxidation-processes in the body. According to the extent of these latter processes, the ratio of the O taken in to the CO₂ given out—*i.e.*, the respiratory quotient—

$$\left(\frac{\text{CO}_2}{\text{O}} = 0.916 \text{ normally}\right) \text{ must vary.}$$

The amount of CO₂ given off may be less than the “mean” above stated. The quantity of CO₂ alone is not a reliable indication of the entire exchange of gases during respiration; we must estimate simultaneously the amount of O absorbed and the CO₂ given off.

Income in 24 hours.	Expenditure in 24 hours.
Oxygen—	Carbonic Acid—
744 grms. = 516500 c.cmtr. (<i>Vierordt</i>).	900 grms. = 455500 c.cmtr. (<i>Vierordt</i>).
[Average, 700 grms.]	36 grms. per hour (<i>Scharling</i>).
	32.8 to 33.4 grms. „ (<i>Liebermeister</i>).
	34 grms. „ „ (<i>Pannum</i>).
	31.5 to 33 grms. „ „ (<i>Ranke</i>).
	[Average, 850 grms. 8 ozs. of carbon.]
	Water— 640 grms. „ „ (<i>Valentin</i>).
	330 „ „ „ (<i>Vierordt</i>).

(At 0° C. and mean barometric pressure).

[**Comparative.**—The following table from Munk shows how the O inspired and the CO₂ expired varies in different animals :—

Species of Animals.	Body-weight in Kilograms.	O Inspired in Grams.	CO ₂ Expired in Grams.
Ox, ...	600.	7950.	10900.
Horse, ...	450.	6100.	9560.
Man, ...	75.	750.	900.
Sheep, ...	70.	820.	1140.
Dog, ...	15.	425.	440.
Cat, ...	2.5	60.	64.
Rabbit, ...	2.	45.	57.
Fowl, ...	1.	31.	39.
Frog, ...	0.03	0.067	0.05]

[**Nitrogen.** The expired air contains a little more N than the air inspired, but the total is only about 7 grams daily, although herbivora eliminate more than carnivora.]

[**Aqueous Vapour** is derived partly from the water (vapour) contained in the inspired air, and partly from the water of the blood circulating in the walls of the respiratory passages.]

126. CONDITIONS INFLUENCING THE GASEOUS EXCHANGES.—The formation of CO₂, in all probability, consists of two distinct processes. First, compounds containing CO₂, which are *oxidation products* of substances containing carbon, seem to be formed in the tissues. The second process consists in the separation of this CO₂, which, however, takes place without the absorption of O. Both processes do not always occur simultaneously, and the one process may exceed the other in extent. The formation and elimination of CO₂ is affected by:—

1. Age.—Until the body is fully developed, the CO₂ given off increases, but it diminishes as the bodily energies decay. Hence, in young persons the O absorbed is relatively greater than the CO₂ given off; at other periods both values are pretty constant. Example:—

Age—Years.	In 24 Hours.	
	CO ₂ Gram. Excreted.=Carbon.	O Absorbed in Grams.
8	443 grams. = 121 Carbon.	375 grams.
15	766 „ = 209 „	652 „
16	950 „ = 259 „	809 „
18–20	1003 „ = 274 „	854 „
20–24	1074 „ = 293 „	914 „
40–60	889 „ = 242 „	757 „
60–80	810 „ = 221 „	689 „

The **absolute amount** of CO₂ given off is less in children than in adults; but if the CO₂ given off be calculated with reference to body-weight, then, weight for weight, a child gives off twice as much CO₂ as an adult.

2. Sex.—Males, from the eighth year onward to old age, give off about one-third more CO₂ than females. This difference is more marked at puberty, when the difference may rise to one-half. After cessation of the menses, there is an increase, and in old age the amount of CO₂ given off diminishes. Pregnancy increases the amount, owing to causes which are easily understood (*Andral and Gavarret*).

3. Constitution.—In general, muscular energetic persons use more O and excrete more CO₂ than less active persons of the same weight.

4. Alternation of Day and Night.—The CO₂ given off is diminished about one-fourth during sleep, due to the constant heat of the surroundings (bed), darkness, absence of muscular activity, and the non-taking of food (see 5, 6, 7, 9). O is not stored up during sleep (*S. Lewin*). After awaking in the morning, the respirations are deeper and more rapid, while the amount of CO₂ given off is increased. It decreases during the forenoon, until dinner at mid-day causes another increase. It falls during the afternoon, and increases again after supper.

During **hybernation**, when no food is taken, and when the respirations cease, or are greatly diminished, the respiratory exchange of gases is carried out by diffusion and the cardio-pneumatic movements (§ 59). The CO₂ given off falls to $\frac{1}{5}$, the O taken in to $\frac{1}{4}$, of what they are in the waking condition. Much less CO₂ is given off than O taken in, so that the body-weight may increase through the excess of O.

5. Temperature of the Surroundings.—Cold-blooded animals become warmer when the temperature of their environment is raised, and they give off more CO₂ in this condition than when they are cooler; *e.g.*, a frog with the temperature of the surroundings at 39° C. excreted three times as much CO₂ as when the temperature was 6° C. **Warm-blooded animals** behave quite differently when the tempera-

ture of the surrounding medium is changed. When the temperature of the animal is lowered thereby, there is a considerable decrease in the amount of CO_2 given off, as in cold-blooded animals, but if the temperature of the animal be increased (and also in fever), the CO_2 is increased (*C. Ludwig and Sanders-Ezn*). Exactly the reverse obtains when the temperature of the surroundings varies, and the bodily temperature remains constant. As the cold of the surrounding medium increases, the processes of oxidation within the body are increased through some as yet unknown reflex mechanism; the number and depth of the respirations increase, whereby more O is taken in and more CO_2 is given out. A man in January uses 32.2 grams O per hour; in July only 31.7 grams. In animals, with the temperature of the surroundings at 8°C ., the CO_2 given off was one-third greater than with a temperature of 38°C . When the temperature of the air increases—the body temperature remaining the same—the respiratory activity and the CO_2 given off diminish, while the pulse remains nearly constant. On passing suddenly from a cold to a warm medium, the amount of CO_2 is considerably diminished; and conversely, on passing from a warm to a cold medium, the amount is considerably increased (§ 214).

6. Muscular Exercise causes a considerable increase in the CO_2 given out, which may be three times greater during walking than during rest (*Ed. Smith*). Ludwig and Sczelkow estimated the O taken in and the CO_2 given off by a rabbit during rest, and when the muscles of the hind limbs were tetanised. During tetanus the O and CO_2 were increased considerably, but in tetanised animals more O was given off in the CO_2 expired than was taken up simultaneously during respiration. The passive animal absorbed nearly twice as much O as the amount of CO_2 given off (§ 294).

7. Taking of food causes a not inconsiderable increase in the CO_2 given off, which depends upon the quantity taken; the increase generally occurs about an hour after the chief meal—dinner. The increased consumption of O following the taking of food into the stomach depends on the increased work of the intestinal tract (*Zuntz and V. Mering*). During **inanition**, the exchange of gases diminishes considerably until death occurs. At first the CO_2 given off diminishes more quickly than the O is taken up. The **quality** of the food influences the CO_2 given off to this extent, that substances rich in carbon (carbohydrates and fats) cause a greater excretion of CO_2 than substances which contain less C (albumins). Regnault and Reiset found that a dog gave off 79 per cent. of the O inspired after a flesh diet, and 91 per cent. after a diet of starch. If easily oxidisable substances (glycerin or lactate of soda) are injected into the blood, the O taken in, and the CO_2 given off, undergo a considerable increase (*Ludwig and Scheremetjewsky*). Alcohols, tea, and ethereal oils diminish the CO_2 (*Prout, Vierordt*). [Ed. Smith divided foods, with reference to the excretion of CO_2 into two classes. The **respiratory excitants** include nitrogenous foods, rum, beer, sugar, stout, &c.; the **non-exciters** starch, fat, some alcoholic mixtures. The most powerful respiratory excitants, however, are tea, sugar, coffee, and rum, and the maximum effect is usually experienced within an hour. He also found that the effects produced by alcoholic drinks varied with the nature of the spirituous liquor. Thus brandy, whisky, and gin diminish the amount; while pure alcohol, rum, ale, and porter tend to increase it.]

A healthy adult, weighing 50 kilos., respire while fasting 8 litres of air per kilo. per hour; he uses 0.4 gram O, and forms 0.5 gram CO_2 . Taking of food increases these numbers to 9 litres, 0.5 gram O, and 0.6 gram CO_2 . The consumption of O is increased about 12 per cent. and the excretion of CO_2 about 27 per cent. after a diet of carbohydrates; it is less with a fatty diet, and least after one of proteids.

8. The number and depth of the respirations have practically no influence on the formation of CO_2 or the oxidation-processes within the body, these being regulated by the tissues themselves, by some mechanism as yet unknown (*Pflüger*).

They have a marked effect, however, upon the elimination of the already formed CO_2 from the body. An increase in the *number* of respirations (their depth remaining the same), as well as an increase of their *depth* (the number remaining the same), causes an *absolute* increase in the amount of CO_2 given off, which, with reference to the total amount of gases exchanged, is *relatively* diminished. The following example from Vierordt illustrates this:—

No. of Resps. per Minute.	Volume of Air.	Amount of CO_2 . = per cent. CO_2 .	Depth of Resps.	Amount of CO_2 . = per cent. CO_2 .
12	6000	258c. emtr. = 4·3 %	500	21 c. emtr. = 4·3 %
24	12000	420 „ = 3·5 „	1000	36 „ = 3·6 „
48	24000	744 „ = 3·1 „	1500	51 „ = 3·4 „
96	48000	1392 „ = 2·9 „	2000	64 „ = 3·2 „
			3000	72 „ = 1·4 „

9. Exposure to a **bright light** causes an increase in the CO_2 given off in frogs, in mammals and birds, even in frogs deprived of their lungs, or in those whose spinal cord has been divided high up. The consumption of O is increased at the same time. The same results occur in blind persons, although to a less degree. Rodents and birds show the maximum in red light, and turtles in violet light. According to Loch, the pupæ of butterflies exposed to light do not produce more CO_2 than those kept in darkness, so that he attributes the greater amount of CO_2 excreted to great muscular exertion produced by the light.

10. The experiments of Gréhan, on dogs, seem to show that intense inflammation of the bronchial mucous membrane influences the CO_2 given off.

11. Amongst **poisons**, thebaïa increases the CO_2 given off, while morphia, eodeia, nareein, narceotin, papaverin, diminish it (*Fübini*).

127. DIFFUSION OF GASES WITHIN THE LUNGS.—The air within the air-vesicles contains most CO_2 and least O, and as we pass from the small to the large bronchi and onwards to the trachea, the composition of the air gradually approaches more closely to that of the atmosphere. Hence, if the air expired be collected in two portions, the first half (*i.e.*, the air from the larger air-passages) contains less CO_2 (3·7 vols. per cent.) than the second half (5·4 vols. per cent.). The difference in the percentage of gases gives rise to a diffusion of the gases within the air-passages; the CO_2 must *diffuse* from the air-vesicles outwards, and the O from the atmosphere and nostrils inwards (§ 33). This movement is aided by the eardio-pneumatic movement (§ 59). In hibernating animals and in persons *apparently* but not actually *dead*, the exchange of gases within the lungs can only occur in the above-mentioned ways. For ordinary purposes this mechanism is insufficient, and there are added the respiratory movements whereby atmospheric air is introduced into the larger air-passages, from which and into which the diffusion currents of O and CO_2 pass, on account of the difference of tension of the gases.

128. EXCHANGE OF GASES IN THE AIR-VESICLES.—The exchange of gases between the gases of the blood and those in the air-vesicles occurs almost exclusively through the agency of chemical processes, and therefore independently of the diffusion of gases.

Method.—It is important to ascertain the tension of the O and CO_2 in the venous blood of the pulmonary capillaries. Pflüger and Wolfberg estimated the tension by “**catheterising the lungs.**” An elastic catheter was introduced through an opening in the trachea of a dog into the bronchus leading to the lowest lobe of the left lung. An elastic sac was placed round the catheter, and when the latter was introduced into the bronchus, the sac around the catheter was distended so as to plug the bronchus. No air could escape between the catheter and the wall of the bronchus. The outer end of the catheter was closed at first, and the dog was

allowed to respire quietly. After four minutes the air in the air-vesicles was completely in equilibrium with the blood-gases. The air of the lung was sucked out of the catheter by means of an air-pump, and afterwards analysed.

Thus we may measure indirectly the tension of the O and CO₂ in the venous blood of the pulmonary capillaries. The *direct* estimation of the gases in different kinds of blood is made by shaking up the blood with another gas. The gases so removed indicate directly the proportion of blood-gases.

The following statement shows the tension and percentage of O and CO₂ in arterial and venous blood, in the atmosphere, and in the air of the alveoli:—

I.	V.
O-Tension in arterial blood=29·6 mm. Hg (corresponding to a mixture containing 3·9 vol. per cent. of O).	O-Tension in the air of the alveoli of the catheterised lung=27·44 mm. Hg (corresponding to 3·6 vol. per cent.).
II.	VI.
CO ₂ -Tension in arterial blood=21 mm. Hg (corresponding to 2·8 vol. per cent.).	CO ₂ -Tension in the air of the alveoli of the catheterised lung=27 mm. Hg (corresponding to 3·56 vol. per cent.).
III.	VII.
O-Tension in venous blood=22 mm. Hg (corresponding to 2·9 vol. per cent.).	O-Tension in the atmosphere=158 mm. Hg (corresponding to 20·8 vol. per cent.).
IV.	VIII.
CO ₂ -Tension in venous blood=41 mm. Hg (corresponding to 5·4 vol. per cent.).	CO ₂ -Tension in the atmosphere=0·38 mm. Hg (corresponding to 0·03–0·05 vol. per cent.).

When we compare the tension of the O in the air (VII. = 158 mm. Hg) with the tension of the O in venous blood (III. = 22 mm. Hg, or V. = 27·44 mm. Hg), we might be inclined to assume that the passage of the O from the air of the air-vesicles into the blood was due solely to diffusion of the gases; and similarly, we might assume that the CO₂ of the venous blood (IV. or VI.) diffused into the air-vesicles, because the tension of the CO₂ in the air is much less (VIII.). There are a number of facts, however, which prove that the exchange of the gases in the lungs is chiefly due to **chemical** forces.

[Von Fleischl finds that fluids yield up their gases very much more easily when they receive a shock, and he regards the shock communicated to the blood, by the contraction of the heart, as an important factor in preparing the blood for the diffusion of CO₂ from the blood-plasma into the lungs. No facts support this theory as applied to the human body.]

[**Changes produced in the Blood by Respiration.**—The blood of the pulmonary artery is changed from venous into arterial blood (§ 39), the most obvious alterations being (1) the change in **colour** from dark crimson to bright scarlet. (2) It loses CO₂. (3) It gains O. (4) The reduced Hb of the venous blood is converted into HbO₂. (5) As to a supposed difference of temperature, see § 209, 3. (6) Pawlow finds that blood which passes several times through the lungs loses its power of coagulation. Are we to assume that the pulmonary tissues have the property of destroying the fibrin-ferment?]

1. **Absorption of O.**—Concerning the absorption of O from the air in the alveoli into the venous blood of the lung-capillaries, whereby the blood is arterialised, it is proved that this is a **chemical process**. The gas-free (reduced) hæmoglobin takes up O to form oxyhæmoglobin (§ 15, 1). That this absorption has nothing to do directly with the diffusion of gases, but is due to a chemical combination of the atomic compounds, is shown by the fact that, when pure O is respired, the blood does not take up more O than when atmospheric air is respired; further, that animals made to breathe in a limited closed space can absorb almost all the O—even to traces—into their blood before suffocation occurs. Of course, if the absorption of O were due to diffusion, in the former case more O would be absorbed, while in the latter case the absorption of O could not possibly occur to such an extent as it does. The law of diffusion comes into play in connection with

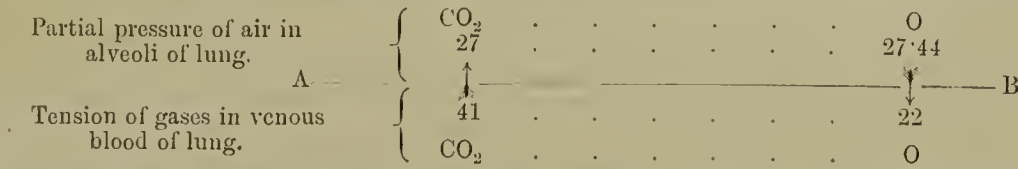
the absorption of O to this extent, viz., that the O diffuses from the air-cells of the lung into the blood-plasma, where it reaches the blood-corpuscles floating in the plasma. The hæmoglobin of the blood-corpuscles forms at once a chemical compound (oxyhæmoglobin) with the O.

Even in **very rarefied air**, such as is met with in the upper regions of the atmosphere during a balloon ascent, the absorption of O still remains independent of the partial pressure. But a much longer *time* is required for this process at the ordinary temperature of the body, so that in rarefied air the absorption of O is greatly delayed, but it is not diminished. This is the cause of death in aeronauts who have ascended so high that the atmospheric pressure is diminished to one-third (*Setchenow*).

2. Elimination of CO₂.—With regard to the excretion of CO₂ from the blood, we must remember that the CO₂ in the blood exists in two conditions. Part of the CO₂ forms a loose or feeble chemical compound, while another portion is more firmly combined. The former is obtained by those means which remove gases from fluids containing them in a state of absorption, so that in removing the CO₂ from the blood it is difficult to determine whether the CO₂, so removed, obeyed the law of diffusion, or if it was expelled by chemical means.

Although it is convenient to represent the excretion of CO₂ from the blood into the air-vesicles of the lung as due to equilibration of the tension of the CO₂ on opposite sides of the alveolar membrane, *i.e.*, to diffusion—nevertheless, **chemical processes** play an important part in this act. The absorption of O by the coloured corpuscles acts, at the same time, in expelling CO₂. This is proved by the fact that the expulsion of CO₂ from the blood takes place more readily when O is simultaneously admitted. The free supply of O not only favours the removal of the CO₂, which is loosely combined, but it also favours the expulsion of that portion of the CO₂ which is more firmly combined, and which can only be expelled by the addition of acids to the blood. That the oxygenated blood-corpuscles (*i.e.*, their oxyhæmoglobin) are concerned in the removal of CO₂ is proved by the fact that CO₂ is more easily removed from serum which contains oxygenated blood-corpuscles than from serum charged with O.

[The following scheme may serve to illustrate the extent to which diffusion comes into play. The O must pass through the alveolar membrane, AB—including the alveolar epithelium and the wall of the capillaries—as well as the blood-plasma, to reach the hæmoglobin of the blood-corpuscles. Similarly, the CO₂ must leave the salts of the plasma with which it is in combination, and diffuse in the opposite direction, through the wall of the capillaries, the alveolar membrane, and epithelium, to reach the air-vesicles. Let AB represent the alveolar membrane; on the one side of it is represented the partial pressure of the CO₂ and O in the air-vesicles; and on the other, the partial pressure of the CO₂ and O in the venous blood entering the lung. The arrows indicate the direction of diffusion.]



Nature of the Process.—The exchange of gases between the blood and the air in the lungs has been represented by Donders as due to the process of **dissociation**.

[Bohr used a modified rheometer of Ludwig's, whereby living arterial blood was brought into direct contact with a volume of air containing a greater or less percentage of CO₂. Even when the amount of CO₂ in the air in direct contact with the blood was very small, it was found that very little CO₂ diffused from the blood into the air-space. Bohr therefore concludes that the separation of CO₂ from the venous blood in the lungs, and its passage into the air-vesicles, are not explicable on the hypothesis of diffusion, but we must rather regard the CO₂ as removed from the blood by the pulmonary tissue by means of a kind of secretory process, analogous to the excretion-processes in glands.]

129. DISSOCIATION OF GASES.—Many gases form *true chemical compounds* with other bodies (*i.e.*, they combine according to their equivalents), when the contact of these bodies is effected under conditions such that the partial pressure of the gases is high. The chemical compound formed under these conditions is broken up whenever the partial pressure is diminished, or when it reaches a certain minimum level, which varies with the nature of the bodies forming the compound. Thus, by increasing and diminishing the partial pressure alternately, a chemical compound of the gas may be formed and again broken up. This process is called **dissociation of the gases**. The minimal partial pressure is constant for each of the different substances and gases, but *temperature*, as in the case of the absorption of gases, has a great effect on the partial pressure; with increase of temperature the partial pressure, under which dissociation occurs, diminishes.

As an example of the dissociation of a gas, take the case of calcium carbonate. When it is heated in the air to 440°C ., CO_2 is given off from its state of chemical combination, but is taken up again, and a chemical compound formed, which is changed into chalk when it cools.

Dissociation in the Blood.—The chemical combinations containing CO_2 and those containing O within the blood-stream, *viz.*, the salts of the plasma, which are combined with CO_2 , and the oxyhæmoglobin, behave in a similar manner. If these compounds of O and CO_2 are placed under conditions where the partial pressure of these gases is very low—*i.e.*, in a medium containing a very small amount of these gases, the compounds are dissociated, *i.e.*, they give off CO_2 or O. If after being dissociated they are placed under conditions where, owing to the large amount of these gases, the partial pressure of O or of CO_2 is high, these gases are taken up again, and enter into a condition of chemical combination.

The hæmoglobin of the blood in the pulmonary capillaries finds plenty of O in the alveoli; hence, it unites with the O owing to the partial pressure of the O in the lung, and so forms the compound oxyhæmoglobin. On its course through the capillaries of the systemic circulation, the oxyhæmoglobin of the blood comes into relation with tissues poor in O; the oxyhæmoglobin is dissociated, the O is supplied to the tissues, and the blood freed from this O returns to the right heart, and passes to the lungs, where it takes up the new O.

The blood whilst circulating meets with most CO_2 in the tissues; the high partial pressure of the CO_2 in the tissues causes CO_2 to unite with certain constituents in the blood so as to form chemical compounds, which carry the CO_2 from the tissues to the lungs. In the air of the lungs, however, the partial pressure of the CO_2 is very low, dissociation of these chemical compounds occurs under the low partial pressure, and the CO_2 passes into the air-cells of the lung, from which it is expelled during expiration. It is evident that the giving up of O from the blood to the tissues, and the absorption of CO_2 from the tissues, go on side by side and take place simultaneously, while in the lungs the reverse processes occur almost simultaneously.

130. CUTANEOUS RESPIRATION.—**Methods.**—If a man or an animal be placed in the chamber of the respiratory apparatus (§ 122), and if tubes be so arranged that the respiratory gases do not enter the chamber, of course we obtain only the “*perspiration*” of the skin in the chamber. It is less satisfactory to leave the head of the person outside the chamber, while the neck is fixed air-tight in the wall of the chamber. The extent of the cutaneous respiration of a limb may be ascertained by enclosing it in an air-tight vessel (*Röhrig*) similar to that used for the arm in the plethysmograph (§ 101).

Loss by Skin.—A healthy man loses by the skin, in 24 hours, $\frac{1}{6}\tau$ of his body-weight, which is greater than the loss by the lungs, in the ratio of 3 : 2. Only 10 grains—150 grains,—or it may be 3.9 grams—60 grains,—of the entire loss are due to the CO_2 given off by the skin. The remainder of the excretion from the skin is due to **water** [$1\frac{1}{2}$ —2lbs. daily] containing a few salts in solution. When the surrounding temperature is raised, the CO_2 is increased, in fact it may be doubled; violent muscular exercise has the same effect

O Absorbed.—The O taken up by the skin is either equal to, or slightly less than, the CO₂ given off. As the CO₂ excreted by the skin is only $\frac{1}{250}$ of that excreted by the lungs, while the O taken in = $\frac{1}{180}$ of that taken in by the lungs, it is evident that the *respiratory activity of the skin is very slight*. Animals whose skin has been covered by an impermeable varnish die, not from suffocation, but from other causes (§ 225).

In animals with a thin moist epidermis (frog) the exchange of gases is much greater, and in them the skin so far supports the lungs in their function, and may even partly replace them functionally. The skin of the frog eliminates $\frac{3}{4}$ – $\frac{2}{3}$ of all the CO₂ excreted (*Bidder*), and even a larger proportion in winter frogs. Thus dipping a frog in oil kills it sooner than ligature of the lungs. In mammals with thick dry cutaneous appendages, the exchange of gases is, again, much less than in man.

131. INTERNAL RESPIRATION.—Where CO₂ is formed.—By the term “internal respiration” is understood the exchange of gases between the capillaries of the systemic circulation and the tissues of the organs of the body. As organic constituents of the tissues, during their activity, undergo gradual oxidation, and form, amongst other products, CO₂; we may assume—(1) that the chief focus for the absorption of O and the formation of CO₂ is to be sought for **within the tissues** themselves. That the O from the blood in the capillaries rapidly penetrates or diffuses into the tissues is shown by the fact that the blood in the capillaries rapidly loses O and gains CO₂, while blood containing O, and kept warm outside the body, changes very slowly and incompletely. If portions of fresh tissues be placed in defibrinated blood containing O, then the O rapidly disappears. Frogs deprived of their blood exhibit an exchange of gases almost as great as normal. This shows that the exchange of gases must take place in the tissues themselves. If the chief oxidations took place in the blood and not in the tissues, then during suffocation, when O is excluded, the substances which use up O, *i.e.*, those substances which act as reducing agents, ought to accumulate in the blood. But this is not the case, for the blood of asphyxiated animals contains mere traces of reducing materials (*Pflüger*). It is difficult to say how the O is absorbed by the tissues, and what becomes of it immediately it comes in contact with the living elements of the tissues. Perhaps it is temporarily stored up, or it may form certain intermediate less oxidised compounds. This may be followed by a period of rapid formation and excretion of CO₂. On this supposition, it is evident that the absorption of O and the excretion of CO₂ need not occur to the same extent, so that the amount of CO₂ given off at any period is not necessarily an index of the amount of O absorbed during the same period (§ 126).

[Oxygen exists in excessively small quantities in the tissues, so that its tension may be considered as nearly zero: thus the O of the blood must diffuse towards the tissues. If two fingers touching each other be held in front of a bright light, then by means of a spectroscope placed opposite the interval between them, one can see the two bands of oxy-hæmoglobin. If the bases of the fingers be constricted the single band of reduced hæmoglobin appears in less than two minutes, so rapidly is the blood robbed of its oxygen. The CO₂ formed in the tissues diffuses towards the blood. The following scheme after Beaunis represents the decrease in tension of the two gases—

O—Atmosphere > air in lungs > blood > tissues.
CO₂—Tissues > blood > air in lungs > atmosphere.]

[There are two views as to where the CO₂ is formed as the blood passes through the tissues. One view is that the seat of oxidation is in the blood itself, and the other is that it is formed in the tissues. If we knew the tension of the gases in the tissues, the problem would be easily solved, but we can only arrive at a knowledge of this subject *indirectly* in the following ways]:—

CO₂ in Cavities.—That the CO₂ is formed in the tissues is supported by the fact that the amount of CO₂ in the fluids of the cavities of the body is greater than the CO₂ in the blood of the capillaries. The tension of CO₂ in—

	Min.		Min.
Arterial blood, . . .	21·28 Hg tension.	Bile (gall bladder), . . .	50·0 Hg tension.
Peritoneal cavity, . . .	58·5 „	Hydrocele fluid, . . .	46·5 „ „
Acid urine, . . .	68·0 „	Lymph (thoracic duct), . . .	34·0 „ „
Cavity of intestine, . . .	58·5 „	(Pflüger and Strassburg.)	

The large amount of CO₂ in these fluids can only arise from the CO₂ of the tissues passing into them.

Gases of Lymph.—The following table shows the amount of gases in lymph:—

	O	CO ₂	N
Lymph from arm, . . . {	0·00	41·89	1·12
	0·10	47·13	1·58
Lymph from intestine, . . .	0·10	37·55	1·63

In the lymph of the ductus thoracicus the tension of CO₂=33·4 to 37·2 mm. Hg, which is greater than in arterial blood, but considerably less than in venous blood (41·0 mm. Hg). (Ludwig and Hammarsten, Tschirjew). This does not entitle us to conclude that in the tissues from which the lymph comes only a small quantity of CO₂ is formed, but rather that in the lymph there is less attraction for the CO₂ formed in the tissues than in the blood of the capillaries, where chemical forces are active in causing it to combine, or that in the course of the long lymph-current, the CO₂ is partly given back to the tissues, or that CO₂ is formed in the blood itself. Further, the muscles, which are by far the largest producers of CO₂, contain few lymphatics, nevertheless they supply much CO₂ to the blood. The amount of free “non-fixed” CO₂ contained in the juices and tissues indicates that the CO₂ passes from the tissues into the blood; still, Preyer believes that in venous blood CO₂ undergoes chemical combination. The exchange of O and CO₂ varies much in the different tissues. The muscles are the most important organs, for in their active condition they excrete a large amount of CO₂, and use up much O. The O is so rapidly used up by them that no free O can be pumped out of muscular tissue (L. Hermann). The exchange of gases is more vigorous during the activity of the tissues. Nor are the salivary glands, kidneys, and pancreas any exception, for although, when these organs are actively secreting, the blood flows out of the dilated veins in a bright red stream, still the relative diminution of CO₂ is more than compensated by the increased volume of blood which passes through these organs.

Reduction by the tissues.—The researches of Ehrlich have shown that in most tissues very energetic reductions take place. If colouring-matters, such as alizarin blue, indophenol blue, or methyl blue, be introduced into the blood-stream, the tissues are coloured by them. Those tissues or organs which have a particular affinity for O (e.g., liver, cortex of the kidney, and lungs), absorb O from these pigments, and render them colourless. The pancreas and submaxillary gland scarcely reduce them at all.

(2) In the **blood itself**, as in all tissues, O is used up and CO₂ is formed. This is proved by the following facts:—That blood withdrawn from the body becomes poorer in O and richer in CO₂; that in the blood of asphyxia, free from O and in the blood-corpuscles, there are slight traces of reducing agents, which become oxidised on the addition of O. Still, this process is comparatively insignificant as against that which occurs in all the other tissues. That the walls of the vessels—more especially the muscular fibres in the walls of the small arteries—use O and produce CO₂ is unquestionable, although the exchange is so slight that the blood in its whole arterial course undergoes no visible change.

Ludwig and his pupils have proved that CO₂ is actually formed in the blood. If the easily oxidisable lactate of soda be mixed with blood, and this blood be caused to circulate in an excised but still living organ, such as a lung or kidney, more O is used up and more CO₂ is formed than in unmixed blood similarly transfused.

(3) That the tissues of the living lungs use O and give off CO₂ is probable. When C. Ludwig and Müller passed arterial blood through the blood-vessels of a lung deprived of air, the O was diminished and the CO₂ increased. As the total

amount of CO_2 and O found in the entire blood, at any one time, is only 4 grams, and as the daily excretion of $\text{CO}_2 = 900$ grams, and the O absorbed daily = 744 grams, it is clear that exchange of gases must go on with great rapidity, that the O absorbed must be used quickly, and the CO_2 must be rapidly excreted.

Still, it is a striking fact that oxidation-processes of such magnitude, as *e.g.*, the union of C to form CO_2 , occur at a relatively low temperature of the blood and the tissues. It has been surmised that the blood acts as an ozone-producer, and transfers this active form of O to the tissues. Liebig showed that the *alkaline reaction* of most of the juices and tissues favours the processes of oxidation. Numerous organic substances, which are not altered by O alone, become rapidly oxidised in the presence of free alkalies, *e.g.*, gallic acid, pyrogallie acid, and sugar; while many organic acids, which are unaffected by ozone alone, are changed into carbonates when in the form of alkaline salts (*Gorup-Besanez*); and in the same way, when they are introduced into the body in the form of acids, they are partly or wholly excreted in the urine, but when they are administered as alkaline compounds they are changed into carbonates.

[**Comparative Physiology of Respiration.**—The most important researches in this department have been made by Regnault and Reiset and Paul Bert. The following table shows the quantity of O absorbed, CO_2 and N excreted by the respiratory organs per kilo.-weight of the animal during one hour:—

	O Absorbed.	CO_2 Excreted.	N Excreted.
	grms.	grms.	grms.
Rabbit, ...	0·883	1·109	0·004
Dog, ...	1·183	1·195	0·007
Marmot, ...	0·986	1·016	0·009
Fowl, ...	1·035	1·368	0·007
Sparrow, ...	9·595	10·583	0·008
Lizard, ...	0·191	0·197	0·004
Frog, ...	0·090	0·091	0·000
Salamander, ...	0·085	0·113	0·000
Cockchafer, ...	0·019	1·137	0·087

[It is evident that the respiration of birds is much more active than that of mammals, while in mammals and insects it is far more active than in reptiles and amphibians. The respiration of fishes is much less active than that of mammals.]

[The **respiratory quotient** shows a marked difference in **carnivora** and **herbivora**; in herbivora = 0·9 – 1, in carnivora = 0·75 – 0·8, while the omnivora, *e.g.*, man, stands midway between = 0·87, but it is increased by carbohydrate food, and diminished by animal food. In starving animals, however, the respiratory quotient is the same = 0·75, showing that the oxidation in starving animals takes place at the expense of the tissues of the body (*Munk*).]

[The **species of animal** exercises a marked influence on the intensity of the respiratory process, as shown by the following table from Munk, giving the amount of O absorbed per unit weight (*i.e.*, per kilogram) of the animal. It is at once apparent that the intensity of respiration is not parallel to the body-weight.

Species of Animal.	O in Grams. Absorbed.	Respiratory Quotient, $\frac{\text{CO}_2}{\text{O}}$.
Cat, ...	1·007	0·77
Dog, ...	1·183	0·75
Rabbit, ...	0·918	0·92
Fowl, ...	1·300	0·93
Small Singing-bird, ...	11·360	0·78
Frog, ...	0·084	0·63
Man, ...	0·417	0·87
Horse, ...	0·563	0·97
Ox, ...	0·552	0·9
Sheep, ...	0·49	0·98

[Small animals, as a rule, have the greatest intensity of respiration; birds have the most intense respiration, and this is greater the smaller the bird. Thus small singing-birds use nearly ten times as much oxygen as fowls. In cold-blooded animals it is exceedingly small. A guinea-pig placed in a chamber containing little oxygen within a short time becomes convulsed and dies, while a frog will live for many hours in an atmosphere devoid of oxygen (*Munk*).]

133. RESPIRATION IN A LIMITED SPACE.—Respiration in a limited space causes—(1) a gradual diminution of O; (2) a simultaneous increase of CO₂, (3) a diminution in the volume of the gases. If the space be of moderate dimensions, the animal uses up almost all the O contained therein, and dies ultimately from spasms caused by the asphyxia. The O is absorbed, therefore—independently of the laws of absorption—by chemical means. The O in the blood is almost completely used up (§ 128). In a larger space, the CO₂ accumulates rapidly, before the diminution of O is such as to affect the life of the animal. As CO₂ can only be excreted from the blood when the tension of the CO₂ in the blood is greater than the tension of CO₂ in the air, as soon as the CO₂ in the surrounding air in the closed space becomes the same as in the blood, the CO₂ will be retained in the blood, and finally CO₂ may pass back into the body. This occurs in a large closed space, when the amount of O is still sufficient to support life, so that death occurs under these circumstances (in rabbits) through poisoning with CO₂ causing diminished excitability, loss of consciousness, and lowering of temperature, but no spasms (*Worm Müller*). In pure O animals breathe in a normal way; the quantity of O absorbed and the CO₂ excreted is quite independent of the percentage of O, so that the former occurs through chemical agency independent of pressure. In a limited space filled with O animals die by absorption of the CO₂ excreted. *Worm Müller* found that rabbits died after absorbing CO₂ equal to half the volume of their body, although the air still contained 50 per cent. O. Animals can breathe quite quietly a mixture of air containing 14·8 per cent. (20·9 per cent. normal); with 7 per cent. they breathe with difficulty; with 4·5 per cent. there is marked dyspnœa; with 3 per cent. O there is tolerably rapid asphyxia. The air expired by man normally contains 14 to 18 per cent. O. According to *Hempner*, mammals placed in a mixture of gases poor in O use slightly less O.

Dyspnœa occurs when the respired air is deficient in O, as well as when it is overcharged with CO₂, but the dyspnœa in the former case is prolonged and severe; in the latter, the respiratory activity soon ceases. The want of O causes a greater and more prolonged increase of the blood-pressure than is caused by excess of CO₂. Lastly, the consumption of O in the body is less affected when the O in the air is diminished than when there is excess of CO₂. If air containing a diminished amount of O be respired, death is preceded by violent phenomena of excitement and spasms, which are absent in cases of death caused by breathing air over-charged with CO₂. In poisoning with CO₂, the excretion of CO₂ is greatly diminished, while with diminution of O it is almost unchanged.

If animals be supplied with a mixture of gases similar to the atmosphere, in which N is replaced by H, they breathe quite normally (*Lavoisier and Seguin*); the H undergoes no great change.

Cl. Bernard found that, when an animal breathed in a limited space, it became partially accustomed to the condition. On placing a bird under a bell-jar, it lived several hours; but if several hours before its death, another bird fresh from the outer air were placed under the same bell-jar, the second bird died soon, with convulsions.

Frogs, when placed for several hours in air devoid of O, give off just as much CO₂ as in air containing O, and they do this without any obvious disturbance. Hence, it appears that the formation of CO₂ is independent of the absorption of O, and the CO₂ must be formed from the decomposition of other compounds. Ultimately, however, complete motor paralysis occurs, whilst the circulation remains undisturbed (*Aubert*).

[**134. DYSPNŒA AND ASPHYXIA.**—For the causes of dyspnœa see § 111, and those of asphyxia see § 368. If from any cause an animal be not supplied

with a due amount of air, normal respiration becomes greatly altered, passing through the phases of **hyperpnœa**, or increased respiration, **dyspnœa**, or difficulty of breathing, to the final condition of suffocation or **asphyxia**. The phenomena of asphyxia may be developed by closing the trachea of an animal with a clamp, or by any means which prevents the entrance of air or blood into the lungs.

The **phenomena of asphyxia** are usually divided into several stages:—1. During the **first stage** there is hyperpnœa, the respirations being deeper, more frequent, and laboured. The extraordinary muscles of respiration—both those of inspiration and expiration (§ 118)—are called into action, dyspnœa is rapidly produced, and the struggle for air becomes more and more severe. At the same time the oxygen of the blood is being used up, while the blood itself becomes more and more venous. The venous blood circulating in the medulla oblongata and spinal cord stimulates the respiratory centres, and causes the violent respirations. This stage usually lasts about a minute, and gradually gives place to—

2. The **second stage**, when the inspiratory muscles become less active, while those concerned in laboured expiration contract energetically, and indeed almost every muscle in the body may contract; so that this stage of violent expiratory efforts ends in general convulsions. The convulsions are due to stimulation of the respiratory centres by the venous blood. The convulsive stage is short, and is usually reached in a little over one minute. This storm is succeeded by—

3. The **third stage**, or stage of exhaustion, the transition being usually somewhat sudden. It is brought about by the venous blood acting on and paralysing the respiratory centres. The pupils are widely dilated, consciousness is abolished, and the activity of the reflex centres is so depressed that it is impossible to discharge a reflex act, even from the cornea. The animal lies almost motionless, with flaccid muscles, and to all appearance dead, but every now and again, at long intervals, it makes a few deep inspiratory efforts, showing that the respiratory centres are not quite, but almost paralysed. Gradually the pauses become longer and the inspirations feebler and of a gasping character. As the venous blood circulates in the spinal cord, it causes a large number of muscles to contract, so that the animal extends its trunk and limbs. It makes one great inspiratory spasm, the mouth being widely opened and the nostrils dilated, and ceases to breathe. After this stage, which is the longest and most variable, the heart becomes paralysed, partly from being over-distended with venous blood, and partly, perhaps, from the action of the venous blood on the cardiac tissues, so that the pulse can hardly be felt. To this pulseless condition the term “asphyxia” ought properly to be applied. In connection with the resuscitation of asphyxiated persons, it is important to note that the heart continues to beat for a few seconds after the respiratory movements have ceased.

The whole series of phenomena occupies from 3 to 5 minutes, according to the animal operated on, and depending also upon the suddenness with which the trachea was closed. If the causes of suffocation act more slowly, the phenomena are the same, only they are developed more slowly.

The Circulation.—The **post-mortem appearances** in man or in an animal are generally well marked. The right side of the heart, the pulmonary artery, the *venæ cavæ*, and the veins of the neck are engorged with dark venous blood. The left side is comparatively empty. If the veins on the right side, or the right side of the heart, be pricked, the blood spurts out. Most observers are agreed that the left side of the heart is comparatively empty, although they are not in accord as to its cause. Some observers ascribe it to the rigor mortis of the left side of the heart, and the elastic recoil of the systemic arteries, forcing the blood towards the systemic veins. G. Johnson ascribes the engorgement of the right side to spasm of the pulmonary arterioles. The **blood** itself is almost black, and is deprived of almost all its oxygen, its hæmoglobin being nearly all in the condition

of reduced hæmoglobin, while ordinary venous blood contains a considerable amount of oxyhæmoglobin as well as reduced Hb. The blood of an asphyxiated animal practically contains none of the former and much of the latter. The **spectrum of blood** from an asphyxiated animal, where all the oxygen has been used up, is that of reduced hæmoglobin (p. 26). It is important to study the changes in the circulation in relation to phenomena exhibited by an animal during suffocation.

We may measure the **blood-pressure** in any artery of an animal while it is being asphyxiated, or we may open its chest, maintain artificial respiration, and place a manometer in a systemic artery, *e.g.*, the carotid, and another in a branch of the pulmonary artery. In the latter case, we can watch the order of events in the heart itself, when the artificial respiration is interrupted. It is well to study the events in both cases.

If the **blood-pressure** be measured in a **systemic artery**, *e.g.*, the carotid, it is found that the blood-pressure rises very rapidly, and to a great extent during the first and second stages; the pulse-beats at first are quicker, but soon become slower and more vigorous. During the third stage it falls rapidly to zero. The great rise of the blood-pressure, during the first and second stages, is chiefly due to the action of the venous blood on the general vaso-motor centre, causing constriction of the small systemic arteries. The peripheral resistance is thus greatly increased, and it tends to cause the heart to contract more vigorously, but the slower and more vigorous beats of the heart are also partly due to the action of the venous blood on the cardio-inhibitory centre in the medulla.

If the second method be adopted, *viz.*, to open the chest, keep up artificial respiration, and measure the blood-pressure in a branch of the pulmonary artery, as well as in a systemic artery,—*e.g.*, the carotid,—we find that when the artificial respiration is stopped, in addition to the rise of the blood-pressure indicated in the carotid manometer, the cavities of the heart and the large veins near it are engorged with venous blood. There is, however, but a slight comparative rise in the blood-pressure in the **pulmonary artery**; while the systemic pressure may be doubled, the pulmonary artery pressure may be only raised a few millimetres (p. 149). This may be accounted for, either by the pulmonary artery not being influenced to the same extent as other arteries by the vaso-motor centre, or by its greater distensibility (§ 88). But, as the heart itself is supplied through the coronary arteries with venous blood, its action soon becomes weakened, each beat becomes feebler, so that soon the left ventricle ceases to contract, and is unable to overcome the great peripheral resistance in the systemic arteries, although the right ventricle may still be contracting. As the blood becomes more venous, the vaso-motor centre becomes paralysed, the small systemic arteries relax, and the blood flows from them into the veins, while the blood-pressure in the carotid manometer rapidly falls. The left ventricle, now relieved from the great internal pressure, may execute a few feeble beats, but they can only be feeble, as its tissues have been subjected to the action of the very impure blood. More and more blood accumulates in the right side from the causes already mentioned. The violent inspiratory efforts in the early stages aspirate blood from the veins towards the right side of the heart, but of course this factor is absent when the chest is opened.]

[**Convulsions** during asphyxia occur only in warm-blooded animals, and not in frogs. If a drug when injected into a mammal excites convulsions, but does not do so in the frog, then it is usually concluded that the convulsions are due to its action on the circulation and respiration, and not to any direct stimulating effect upon the motor centres. But if the drug excites convulsions both in the mammal and frog, then it probably acts directly on the motor centres (*Brunton*).]

[**Recovery from the condition of Asphyxia.**—If the trachea of a dog be closed suddenly and completely, the average duration of the respiratory movements is 4 minutes 5 seconds, while

the heart continues to beat for about 7 minutes. Recovery may be obtained if proper means be adopted before the heart ceases to beat ; but after this, never. If a dog be drowned, the result is different. After complete submersion for $1\frac{1}{2}$ minute, recovery did not take place. In drowning, air passes out of the chest, and water is inspired into and fills the air-vesicles. It is rare for recovery to take place in a person deprived of air for more than five minutes. If the statements of sponge-divers are to be trusted, a person may become accustomed to the deprivation of air for a longer time than usual. In cases where recovery takes place after a much longer period of submersion, it has been suggested that, in these cases, syncope occurs, the heart beats but feebly or not at all, so that the oxygen in the blood is not used up with the same rapidity. It is a well-known fact that newly-born and young puppies can be submerged for a long time before they are suffocated. Young mammals in which the eyes remain closed for some time after birth survive submersion for a much longer time than the same class of animals a few days older, the reason being that in the former the foramen ovale and ductus arteriosus are still patent, while in the latter they are closed.]

Artificial Respiration in Asphyxia.—In cases of suspended animation, *artificial respiration* must be performed. The first thing to be done is to remove any foreign substance from the respiratory passages (mucus or cedematous fluids) in the newly-born or asphyxiated. In doubtful cases, open the trachea and suck out any fluid by means of an elastic catheter (*v. Hüter*). Recourse must in all cases be had to artificial respiration. There are several methods of dilating and compressing the chest so as to cause an exchange of gases. One method is to compress the chest rhythmically with the hands.

[**Marshall Hall's Method.**—“After clearing the mouth and throat, place the patient on the face, raising and supporting the chest well on a folded coat or other article of dress. Turn the body very gently on the side and a little beyond, and then briskly on the face, back again, repeating these measures cautiously, efficiently, and perseveringly, about fifteen times in the minute, or once every four or five seconds, occasionally varying the side. By placing the patient on the chest, the weight of the body forces the air out ; when turned on the side this pressure is removed, and air enters the chest. On each occasion that the body is replaced on the face, make uniform but efficient pressure with brisk movement on the back between and below the shoulder-blades or bones on each side, removing the pressure immediately before turning the body on the side. During the whole of the operations let one person attend solely to the movements of the head and of the arm placed under it.”]

[**Sylvester's Method.**—“Place the patient on the back on the flat surface, inclined a little upwards from the feet ; raise and support the head and shoulders on a small firm cushion or folded article of dress placed under the shoulder-blades. Draw forward the patient's tongue, and keep it projecting beyond the lips ; an elastic band over the tongue and under the chin will answer this purpose, or a piece of string or tape may be tied round them, or by raising the lower jaw the teeth may be made to retain the tongue in that position. Remove all tight clothing from about the neck and chest, especially the braces.” “*To Imitate the Movements of Breathing.*—Standing at the patient's head, grasp the arms just above the elbows, and draw the arms gently and steadily upwards above the head, and *keep them stretched upwards* for two seconds. By this means air is drawn into the lungs. Then turn down the patient's arms, and press them gently and firmly for two seconds against the sides of the chest. By this means air is pressed out of the lungs. Repeat these measures alternately, deliberately, and perseveringly about fifteen times in a minute, until a spontaneous effort to respire is perceived, immediately upon which cease to imitate the movements of breathing, and proceed to *induce circulation and warmth.*”]

Howard advises rhythmical compression of the chest and abdomen by sitting like a rider astride of the body, while Schüller advises that the lower ribs be seized from above with both hands and raised, whereby the chest is dilated, especially when the thigh is pressed against the abdomen to compress the abdominal walls. The chest is compressed by laying the hands flat upon the hypochondria. Artificial respiration acts favourably by supplying O to, as well as removing CO₂ from, the blood ; further, it aids the movement of the blood within the heart and in the large vessels of the thorax. If the action of the heart has ceased, recovery is impossible. In asphyxiated newly-born children, we must not cease too soon to perform artificial respiration. Even when the result appears hopeless, we ought to persevere. Pflüger and Zuntz observed that the reflex excitability of the fetal heart continued for *several* hours after the death of the mother.

Resuscitation by compressing the heart.—Böhm found that in the case of cats poisoned with potash salts or chloroform, or asphyxiated, so as to arrest respiration and the action of the heart,—even for a period of forty minutes,—and even when the pressure within the carotid had fallen to zero, he could restore animation by *rhythmical compression of the heart*, combined with artificial respiration. The compression of the heart causes a slight movement of the blood, while it acts at the same time as a rhythmical cardiac stimulus. After recovery of the respiration, the reflex excitability and gradually also voluntary movements are restored. The animals are blind for several days, the brain acts slowly, and the urine contains sugar. These experiments show how important it is in cases of asphyxia to act at the same time upon the heart.

For physiological purposes, artificial respiration is often made use of, especially after poisoning with curare. Air is forced into the lungs by means of an elastic bag or bellows, attached to a cannula tied in the trachea. The cannula has a small opening in the side of it to allow the expired air to escape.

Pathological.—After the lungs have once been properly distended with air, it is impossible by any amount of direct compression of them to get rid of all the air. This is probably due to the pressure acting on the small bronchi, so as to squeeze them, before the air can be forced out of the air-vesicles. If, however, a lung be filled with CO_2 , and be suspended in water, the CO_2 is absorbed by the water, and the lungs become quite free from air and are *atelectatic* (*Hermann and Keller*). The atelectasis, which sometimes occurs in the lung, may thus be explained:—If a bronchus is stopped with mucus or exudation, CO_2 accumulates in the air-vesicles belonging to this bronchus. If the CO_2 is absorbed by the blood or lymph, the corresponding area of the lung will become atelectatic. Sometimes there is spasm of the respiratory muscles, brought about by direct or reflex stimulation of the respiratory centre.

135. RESPIRATION OF FOREIGN GASES.—No gas without a sufficient admixture of O can support life. Even with completely innocuous and indifferent gases, if no O be mixed with them, they cause suffocation in 2 to 3 minutes.

I. Completely indifferent Gases are N, H, CH_4 . The living blood of an animal breathing these gases yields no O to them (*Pflüger*).

II. Poisonous Gases.—**O-displacing Gases.**—(a) Those that displace O, and form a stable compound with the hæmoglobin—(1) CO (§§ 16 and 17). (2) CNH (hydrocyanic acid) displaces (?) O from hæmoglobin, forming a more stable compound, and kills exceedingly rapidly. Blood-corpuscles charged with hydrocyanic acid lose the property of decomposing hydric peroxide into water and O (§ 17, 5).

(b) **Narcotic Gases.**—(1) CO_2 .—V. Pettenkofer characterises atmospheric air containing 1 per cent. CO_2 as “bad air”; still, air in a room containing this amount of CO_2 produces a disagreeable feeling, rather from the impurities mixed with it than from the actual amount of CO_2 itself. Air containing 1 per cent. CO_2 produces decided discomfort, and with 10 per cent. it endangers life, while larger amounts cause death, with symptoms of coma. (2) N_2O (nitrous oxide), respired, mixed with $\frac{1}{2}$ volume O, causes, after 1 to 2 minutes, a short temporary stage of excitement (“Laughing gas” of H. Davy), which is succeeded by unconsciousness, and afterwards by an increased excretion of CO_2 . (3) Ozonised air causes similar effects (*Binz*).

(c) **Reducing Gases.**—(1) H_2S (sulphuretted hydrogen) rapidly robs blood-corpuscles of O—S and H_2O being formed—and death occurs rapidly before the gas can decompose the hæmoglobin to form a sulphur-methæmoglobin compound. (2) PH_3 (phosphuretted hydrogen) is oxidised in the blood to form phosphoric acid and water, with decomposition of the hæmoglobin.

(3) AsH_3 (arseniuretted hydrogen) and SbH_3 (antimoniuretted hydrogen) act like PH_3 , but the hæmoglobin passes out of the stroma and appears in the urine.

(4) C_2N_2 (cyanogen) absorbs O, and decomposes the blood.

III. Irrespirable gases, i.e., gases which, on entering the larynx, cause reflex spasm of the glottis. When introduced into the trachea, they cause inflammation and death. Under this category come hydrochloric, hydrofluoric, sulphurous, nitrous, and nitric acids, ammonia, chlorine, fluorine, and ozone.

136. ACCIDENTAL IMPURITIES OF THE AIR.—Amongst these are **dust-particles**, which occur in enormous amount suspended in the air, and thereby act injuriously upon the respiratory organs. The **ciliated epithelium** of the respiratory passages eliminates a large number of them. Some of them, however, reach the air-vesicles of the lung, where they penetrate the epithelium, reach the interstitial lung-tissue and lymphatics, and so pass with the lymph-stream into the bronchial glands. Particles of *coal* or *charcoal* are found in the lungs of all elderly individuals, and blacken the alveoli. In moderate amount, these black particles do not seem to do any harm in the tissues, but when there are large accumulations they give rise to lung-affections, which lead to disintegration of these organs. [In coal-miners, for example, the lung-tissues along the track of the lymphatics and in the bronchial glands are quite black, constituting “coal-miners’ lung.”] The lymphatics of the mediastinal pleura can only take up such pigment as reaches them from the pleural cavities (*Fleiner*). In **many trades** various particles occur in the air; miners, grinders, stone-masons, file-makers, weavers, spinners, tobacco manufacturers, millers, and bakers suffer from lung affections caused by the introduction of particles of various kinds inhaled during the time they are at work.

Germ and Micro-organisms.—There seems no doubt that the seeds of some contagious diseases may be inhaled. Diphtheritic bacteria (*Bacillus diphtheriæ*) become localised in the pharynx and in the larynx—glanders in the nose—measles in the bronchi—whooping-cough in the bronchi—hay-monads in the nose—the *Bacillus pneumoniae* of pneumonia in the pulmonary alveoli. Tuberculosis, according to R. Koch, is due to the introduction and development of the *Bacillus tuberculosis* in the lungs, the bacillus being derived from the dust of tuberculous sputa. The same seems to be the case with the *Bacillus* of leprosy and with *Bacillus malariae*, which is the cause of malaria. The latter organism, *Plasmodium malariae*, is endowed with amœboid movements, and thus passes from the respiratory organs into the blood, and changes the Hb within the red blood-corpuscles into melanin (§ 10, 3), and causes them to break up (*Marchiafava and Celli*). The *Micrococcus vaccinae* of small-pox gains access to the blood in the same way, also the *Spirillum* of remittent fever (fig. 32), the microbe of scarlet fever, &c.

Seeds of disease passing into the mouth along with air, and also with the food, are swallowed, and undergo development in the intestinal tract, as is probably the case in cholera (*Comma bacillus* of *R. Koch*), dysentery, typhoid, and anthrax, the last of which is due to *Bacterium anthracis*.

137. VENTILATION OF ROOMS.—Fresh air is as necessary for the healthy as for the sick. Every healthy person ought to have a cubic space of at the very least 800 cubic feet, and every sick person at the very least 1000 cubic feet of space. [The cubic space allowed per individual varies greatly, but 1000 cubic feet is a fair average. If the air in this space is to be kept sweet, so that the CO_2 does not exceed .06 per cent., 3000 cubic feet of air per hour must be supplied, *i.e.*, the air in the space must be renewed three times per hour.]

[**Floor-Space.**—It is equally important to secure sufficient floor-space, and this is especially the case in hospitals. If possible, 100–120 square feet of floor-space ought to be provided for each patient in a hospital-ward, and if it is obtainable a cubic space of 1500 cubic feet (*Parkes*). In all cases the minimum floor-space should not be less than $\frac{1}{4}$ of the cubic space.]

Overcrowding.—When there is overcrowding in a room, the amount of CO_2 increases. V. Pettenkofer found the normal amount of CO_2 (.04 to .05 per 1000) increased in comfortable rooms to 0.54–0.7 per 1000; in badly ventilated sick-chambers = 2.4; in overcrowded auditoriums, 3.2; in pits = 4.9; in schoolrooms, 7.2 per 1000. Although it is not the quantity of CO_2 which makes the air of an overcrowded room injurious, but the excretions from the outer and inner surfaces of the body, which give a distinct odour to the air, quite recognisable by the sense of smell, still the amount of CO_2 is taken as an index of the presence and amount of these other deleterious substances. Whether or not the ventilation of a room or ward occupied by persons is sufficient, is ascertained by estimating the amount of CO_2 . A room which does not give a disagreeable, somewhat stuffy, odour has less than 0.7 per 1000 of CO_2 , while the ventilation is certainly insufficient if the CO_2 = 1 per 1000. As the air contains only 0.0005 cubic metre CO_2 in 1 cubic metre of air, and as an adult produces hourly 0.0226 cubic metre CO_2 , calculation shows that every person requires 113 cubic metres of fresh air per hour, if the CO_2 is not to exceed 0.7 per 1000: for $0.7 : 1000 = (0.0226 + x \times 0.0005) : x$, *i.e.*, $x = 113$.

[**Vitiating Products.**—In a state of repose, an adult man gives off from 12 to 16 cubic feet of CO_2 in twenty-four hours, or on an average .6 cubic feet per hour. To this must be added a certain quantity of organic matter, which is extremely deleterious to health. While the CO_2 diffuses readily and is easily disposed of by opening the windows, this is not the case with the organic matter, which adheres to clothing, curtains, and furniture; hence to get rid of it, a room, and especially a sleeping apartment, requires to be well aired for a long time, together with the free admission of sunlight. We must also remember that an adult gives off from 25 to 40 oz. of water by the skin and lungs. The nature of the organic matters is not precisely known, but some of it is particulate, consisting of epithelium, fatty matters, and organic vapours from the lungs and mouth. It blackens sulphuric acid, and decolourises a weak solution of potassic permanganate. As a test, if we expire through distilled water, and this water be set aside for some time in a warm place, it will soon become fetid. We must also take into consideration the products of combustion; thus 1 cubic foot of coal-gas, when burned, destroys all the O in 8 cubic feet of air (*Parkes*).]

Methods.—In ordinary rooms, where every person is allowed the necessary cubic space (1000 cubic feet), the air is sufficiently renewed by means of the pores in the walls of the room, by the opening and shutting of doors, and by the fireplace, provided the damper is kept open. It is

most important to notice that the natural ventilation be not interfered with by dampness of the walls, for this influences the pores very greatly. At the same time, damp walls are injurious to health by conducting away heat, and in them the germs of infectious diseases may develop.

[Natural Ventilation.]—By this term is meant the ventilation brought about by the ordinary forces acting in nature; such as diffusion of gases, the action of winds, and the movements excited owing to the different densities of air at unequal temperatures.]

[Artificial Ventilation.]—Various methods are in use for ventilating public buildings and dwelling-houses. Two principles are adopted for the former, viz., **extraction** and **propulsion of air**. In the former method, the air is sucked out of the rooms by a fan or other apparatus, while in the latter, air is forced into the rooms, the air being previously heated to the necessary temperature.]

[Tobin's Tubes, placed in the walls, furnish a very convenient method of introducing air into a room. The air enters through these tubes from the outside near the floor, and is carried up six or more feet, to an opening in the wall; the cool air thus descends slowly. For a sitting-room, a convenient plan of window ventilation is **H. Bird's Method**:—Raise the lower sash and place under it, so as to fill up the opening, a piece of wood 3 or 4 inches high. Air will then pass in, in an upward direction, between the upper part of the lower sash-frame and the lower part of the upper one.]

138. FORMATION OF MUCUS, SPUTUM.—The respiratory mucous membrane is covered normally with a thin layer of mucus (fig. 147, *a*). It so far inhibits the formation of new mucus by protecting the mucous glands from the action of cold or other irritative agents. New mucus is secreted as that already formed is removed. An increased secretion accompanies congestion of the respiratory mucous membrane [or any local irritation]. Division of the nerves on one side of the trachea (cat) causes redness of the tracheal mucous membrane and increased secretion (*Rossbach*), [but the two processes do not stand in the relation of cause and effect]. The secretion cannot be excited by stimulating the nerves going to the mucous membrane. [This merely causes anæmia of the mucous membrane, while the secretion continues.]

Modifying Conditions.—If ice be placed on the belly of an animal so as to cause the animal “to take a cold,” the respiratory mucous membrane first becomes pale, and afterwards there is a copious mucous secretion, the membrane becoming deeply congested. The injection of sodium carbonate and ammonium chloride into the blood limits the secretion. The local application of alum, silver nitrate, or tannic acid, makes the mucous membrane turbid, and the epithelium is shed. The secretion is excited by apomorphin, emetin, pilocarpin, and ipecacuanha when given internally, while it is limited by atropin and morphia (*Rossbach*).

[Expectorants favour the removal of the secretions from the air-passages. This they may do either by (*a*) altering the character and qualities of the secretion itself, or (*b*) by affecting the expulsive mechanism. Some of the drugs already mentioned are examples of the first class. The second class act chiefly by influencing the respiratory centre, *e.g.*, ipecacuanha, strychnia, ammonia, senega; emetics also act energetically as expectorants, as in some cases of chronic bronchitis; warmth and moisture in the air are also powerful adjuncts.]

Sputum.—Under normal circumstances, some mucus—mixed with a little saliva—may be coughed up from the back of the throat. In catarrhal conditions of the respiratory mucous membrane, the sputum is greatly increased in amount, and is often mixed with other characteristic products. **Microscopically**, sputum contains—

1. **Epithelial Cells**, chiefly squames from the mouth and pharynx (fig. 171), more rarely alveolar epithelium and ciliated epithelium (7) from the respiratory passages. They are often altered owing to maceration or other changes. Thus some cells may have lost their cilia (6).

The **epithelium of the alveoli** (2) is squamous epithelium, the cells being two to four times the breadth of a colourless blood-corpuscle. These cells occur chiefly in the morning sputum in individuals over 30 years of age. In younger persons their presence indicates a pathological condition of the pulmonary parenchyma.

They often undergo fatty degeneration, and they may contain pigment-granules (3); or they may present the appearance of what Buhl has called “*myelin degenerated cells*,” *i.e.*, cells filled with clear refractive drops of various sizes, some colourless, others with coloured particles, the latter having been absorbed (4). Mucin in the form of myelin drops (5) is always present in sputum.

2. **Lymphoid cells** (9) are colourless blood-corpuscles which have wandered out of the blood-vessels ; they are most numerous in yellow sputum, and less numerous in the clear mucus-like excretion. The lymph-cells often present alterations in their characters ; they may be shrivelled up, fatty, or present a granular appearance.

The **fluid substance** of the sputum contains much **mucus**, arising from the mucous glands and goblet cells, together with nuelein, and lecithin, and the constituents of saliva, according to the amount of the latter mixed with the secretion. *Albumin* occurs only during the inflammation of the respiratory passages, and its amount increases with the degree of inflammation. Urea has been found in cases of nephritis.

In cases of **catarrh**, the sputum is at first usually sticky and clear (*sputa cruda*), but later it becomes more firm and yellow (*sputa cocta*). Under **pathological conditions**, there may be found



Fig. 171.

Various objects found in sputum. 1, detritus and particles of dust ; 2, alveolar epithelium with pigment ; 3, fatty and pigmented alveolar epithelium ; 4, alveolar epithelium with myelin-forms ; 5, free myelin-forms ; 6, 7, ciliated epithelium, some without cilia ; 8, squamous epithelium from the mouth ; 9, leucocytes ; 10, elastic fibres ; 11 fibrin-cast of a small bronchus ; 12, *leptothrix buccalis* with cocci, bacteria, and spirochaetæ ; *a*, fatty acid crystals and free fatty granules ; *b*, hæmatoidin ; *c*, Charcot's crystals ; *d*, cholesterol.

in the sputum—(*a*) red blood-corpuscles from rupture of a blood-vessel. (*b*) **Elastic fibres** (10) from disintegration of the alveoli of the lung ; usually the bundles are fine, curved, and the fibres branched. [In certain cases it is well to add a solution of caustic potash, which dissolves most of the other elements, leaving the elastic fibres untouched.] Their presence always indicates destruction of the lung tissue. (*c*) Colourless plugs of **fibrin** (11), casts of the smaller or larger bronchi, occur in some cases of fibrinous exudation into the finer air-passages. (*d*) **Crystals** of various kinds—crystals of *fatty acids* in bundles of fine needles (fig. 171, *a*). They indicate great decomposition of the stagnant secretion. Leucin and tyrosin crystals are rare (§ 269). Tyrosin occurs in considerable amount when an old abscess breaks into the lungs. Colourless, sharp-pointed, octagonal or rhombic plates—**Charcot's crystals** (*c*)—have been found in the expectoration in asthma, and exudative affections of the bronchi. **Hæmatoidin** (*b*) and **cholesterin** crystals (*d*) occur much more rarely.

Fungi and other lowly organisms are taken in during inspiration (§ 136). The threads of *Leptothrix buccalis* (12), detached from the teeth, are frequently found (§ 147). Mycelium and

spores are found in thrush (*Oidium albicans*), especially in the mouths of sucking infants. In malodorous expectoration rod-shaped bacteria are present. In pulmonary gangrene are found monads, and coccimonads; in pulmonary phthisis the tubercle bacillus; very rarely sarcina, which, however, is often found in gastric catarrh in the stomach and also in the urine (§ 270).

Physical Characters.—Sputum, with reference to its physical characters, is described as *mucous*, *mucopurulent*, or *purulent*.

Abnormal coloration of the sputum—red from blood; when the blood remains long in the lung it undergoes a regular series of changes, and tinges the sputum dark-red, bluish-brown, brownish-yellow, a prune-juice tint, deep yellow, yellowish-green, or grass-green. The sputum is sometimes yellow in jaundice. The sputum may be tinged by what is inspired [as in the case of the “black-spit” of miners].

The odour of the sputum is more or less unpleasant. It becomes very disagreeable when it has remained long in pathological lung-cavities, and it is stinking in gangrene of the lung.

139. ACTION OF THE ATMOSPHERIC PRESSURE.—At the normal pressure of the atmosphere (height of the barometer, 760 millimetres Hg), pressure is exerted upon the entire surface of the body = 15,000 to 20,000 kilos., according to the extent of the superficial area. This pressure acts equally on all sides upon the body, and also occurs in all *internal cavities containing air*, both those that are constantly filled with air (the respiratory passages and the spaces in the superior maxillary, frontal, and ethmoid bones), and those that are temporarily in direct communication with the outer air (the digestive tract and tympanum). As the **fluids of the body** (blood, lymph, secretions, parenchymatous juices) are practically incompressible, their volume remains unchanged under the pressure; but they absorb gases from the air corresponding to the prevailing pressure (*i.e.*, the partial pressure of the individual gases), and according to their temperature (§ 33). The **solids** consist of elementary parts (cells and fibres), each of which presents only a microscopic surface to the pressure, so that for each cell the prevailing pressure of the air can only be calculated at a few millimetres—a pressure under which the most delicate histological tissues undergo development. As an example of the action of the pressure of the atmospheric pressure upon large masses, take that brought about by the adhesion of the smooth, sticky, moist, articular surfaces of the shoulder and hip-joints; the arm and the leg are supported without the action of muscles. The thigh-bone remains in its socket after section of all the muscles and its capsule. Even when the cotyloid cavity is perforated, the head of the femur does not fall out of its socket. The ordinary barometric variations affect the respiration—a rise of the barometric pressure excites, while a fall diminishes the respirations. The absolute amount of CO_2 remains the same (§ 126, 8).

Great diminution of the atmospheric pressure, such as occurs in ballooning (highest ascent, 8600 metres), or in ascending mountains, causes a series of characteristic phenomena:—(1) In consequence of the diminution of the pressure upon the parts directly in contact with the air, they become greatly congested, hence there is redness and swelling of the skin and free mucous membranes; there may be hæmorrhage from the nose, lungs, gums; turgidity of the cutaneous veins; copious secretion of sweat; great secretion of mucus. (2) A feeling of weight in the limbs, a pressing outwards of the tympanic membrane (until the tension is equilibrated by opening the Eustachian tube), and as a consequence noises in the ears and difficulty of hearing. (3) In consequence of the diminished tension of O in the air (§ 128), there is difficulty of breathing, pain in the chest, whereby the respirations (and pulse) become more rapid, deeper, and irregular. When the atmospheric pressure is diminished $\frac{1}{2}$ – $\frac{1}{3}$, the amount of O in the blood is diminished, the CO_2 is imperfectly removed from the blood, and in consequence there is diminished oxidation within the body. When the atmospheric pressure is diminished to one-half, the amount of CO_2 in arterial blood is lessened; and the amount of N diminishes proportionally with the decrease of the atmospheric pressure. The diminished tension of the air prevents the vibrations of the vocal

cords from occurring so forcibly, and hence the voice is feeble. (5) In consequence of the amount of blood in the skin, the internal organs are relatively anæmic; hence, there is diminished secretion of urine, muscular weakness, disturbances of digestion, dulness of the senses, and it may be unconsciousness, and all these phenomena are intensified by the conditions mentioned under (3). Some of these phenomena are modified by usage. The highest limit at which a man may still retain his senses is placed by Tissandier at an elevation of 8000 metres (280 mu. Hg). In dogs the blood-pressure falls, and the pulse becomes small and diminished in frequency, when the atmospheric pressure falls to 200 mm. Hg.

Those who live upon high mountains suffer from a disease, "*mal de montagne*," which consists essentially in the above symptoms, although it is sometimes complicated with anæmia of the internal organs. Al. v. Humboldt found that in those who lived on the Andes the thorax was capacious. At 6000 to 8000 feet above sea-level, water contains only one-third of the absorbed gases, so that fishes cannot live in it. Animals may be subjected to a further diminution of the atmospheric pressure by being placed under the receiver of an air-pump. Birds die when the pressure is reduced to 120 mm. Hg; mammals at 40 mm. Hg; frogs endure repeated evacuations of the receiver, whereby they are much distended, owing to the escape of gases and water, but after the entrance of air they become greatly compressed. The cause of death in mammals is ascribed by Hoppe-Seyler to the evolution of bubbles of gas in the blood; these bubbles stop up the capillaries, and the circulation is arrested. *Local diminution of the atmospheric pressure* causes marked congestion and swelling of the part, as occurs when a cupping-glass is used.

Great increase of the atmospheric pressure causes phenomena, for the most part, the reverse of the foregoing, as in pneumatic cabinets and in diving-bells, where men may work even under $4\frac{1}{2}$ atmospheres pressure. (1) Paleness and dryness of the external surfaces, collapse of the cutaneous veins, diminution of perspiration, and mucous secretions. (2) The tympanic membrane is pressed inwards (until the air escapes through the Eustachian tube, after causing a sharp sound), acute sounds are heard, pain in the ears, and difficulty of hearing. (3) A feeling of lightness and freshness during respiration, the respiration becomes slower (by 2-4 per minute), inspiration easier and shorter, expiration lengthened, the pause distinct. The capacity of the lungs increases, owing to the freer movement of the diaphragm, in consequence of the diminution of the intestinal gases. Owing to the more rapid oxidations in the body, muscular movement is easier and more active. The O absorbed and the CO₂ excreted are increased. The venous blood is reddened. (4) Difficulty of speaking, alteration of the tone of the voice, inability to whistle. (5) Increase of the urinary secretion, more muscular energy, more rapid metabolism, increased appetite, subjective feeling of warmth, pulse beats slower, and pulse-curve is lower (compare § 74). In animals subjected to excessively high atmospheric pressure, P. Bert found that the arterial blood contained 30 vols. per cent. O (at 760 mm. Hg); when the amount rose to 35 vols. per cent., death occurred with convulsions. Compressed air has been used for therapeutical purposes, but in doing so a too rapid increase of the pressure is to be avoided. Waldenburg has constructed such an apparatus, which may be used for the respiration of air under a greater or less pressure.

Frogs, when placed in compressed O (at 14 atmospheres) exhibit the same phenomena as if they were in a vacuum, or pure N. There is paralysis of the central nervous system, sometimes preceded by convulsions. The heart ceases to beat (not the lymph hearts), while the excitability of the motor nerves is lost at the same time, and lastly the direct muscular excitability disappears. An excised frog's heart placed in O under a very high pressure (13 atmospheres) scarcely beats one-fourth of the time during which it pulsates in air. If the heart be exposed to the air again it begins to beat so that compressed O renders the vitality of the heart latent before abolishing it.

Phosphorus retains its luminosity under a high pressure in O, but this is not the case with the luminous organisms, *e.g.*, *Lampyrus*, and luminous bacteria. High atmospheric pressure is also injurious to plants.

140. COMPARATIVE AND HISTORICAL.—**Mammals** have lungs similar to those of man. The lungs of **birds** are spongy, and united to the chest-wall, while there are openings on their

surface communicating with thin-walled "air-sacs," which are placed amongst the viscera. The air-sacs communicate with cavities in the bones, which give the latter great lightness. The diaphragm is absent. In reptiles the lungs are divided into greater and smaller compartments; in snakes one lung is abortive, while the other has the elongated form of the body. The amphibians (frog) possess two simple lungs, each of which represents an enormous infundibulum with its alveoli. The frog pumps air into its lungs by the contraction of its throat, the nostrils being closed and the glottis opened. When young—until their metamorphosis—frogs breathe like fishes by means of gills. The perennibranchiate amphibians (Protens) retain their gills throughout life. Amongst fishes which breathe by gills and use the O absorbed by the water, the Dipnoi have in addition to gills a swim-bladder provided with afferent and efferent vessels, which is comparable to the lung. The Cobitis respire also with its intestine. Insects and centipedes respire by "tracheæ," which are branched canals distributed throughout the body; they open on the surface of the body by openings (stigmata) which can be closed. Spiders respire by means of tracheæ and tracheal sacs, crabs by gills. The molluscs and cephalopods have gills; some gasteropods have gills and others lungs. Amongst the lower invertebrata some breathe by gills, others by means of a special "water-vascular system," and others again by no special organs.

Historical.—Aristotle (384 B.C.) regarded the object of respiration to be the cooling of the body, so as to moderate the internal warmth. He observed correctly that the warmest animals breathe most actively, but in interpreting the fact he reversed the cause and effect. Galen (131–203 A.D.) thought that the "soot" was removed from the body along with the expired water. The most important experiments on the mechanics of respiration date from Galen; he observed that the lungs passively follow the movements of the chest; that the diaphragm is the most important muscle of inspiration; that the external intercostals are inspiratory; and the internal, expiratory. He divided the intercostal nerves and muscles, and observed that loss of voice occurred. On dividing the spinal cord higher and higher, he found that as he did so the muscles of the thorax lying higher up became paralysed. Oribasius (360 A.D.) observed that in double pneumothorax both lungs collapsed. Vesalius (1540) first described artificial respiration as a means of restoring the beat of the heart. Malpighi (1661) described the structure of the lungs. J. A. Borelli († 1679) gave the first fundamental description of the mechanism of the respiratory movements. The chemical processes of respiration could only be known after the discovery of the individual gases therein concerned. Van Helmont († 1644) detected CO_2 . [Joseph Black (1757) discovered that CO_2 , or "fixed air," is given out during expiration.] In 1774 Priestley discovered O. Lavoisier detected N (1775), and ascertained the composition of atmospheric air, and he regarded the formation of CO_2 and H_2O of the breath as a result of a combustion within the lungs themselves. J. Ingen-Houss (1730–1799) discovered the respiration of plants. Vogel and others proved the existence of CO_2 in venous blood, and Hoffmann and others that of O in arterial blood. The more complete conception of the exchange of gases was, however, only possible after Magnus had extracted and analysed the gases of arterial and venous blood (§ 36).

Physiology of Digestion.

[The substances which are used as food—the **food-stuffs** or **alimentary principles** belong to several different groups and may be conveniently classified as—

1. Proteids or albuminous bodies.
2. Carbohydrates.
3. Fats.
4. Mineral or saline bodies, and water.

Some of these bodies are insoluble in water, and others do not readily pass through animal membranes in their unaltered condition. As the food is carried along the alimentary canal it is subjected to the action of certain juices which are formed by the secretory activity of the cells lining the alimentary canal or by the glands which open into it. These juices (saliva, gastric juice, pancreatic juice, bile, and the secretions of the small and large intestine) are formed in **glands** (fig. 172), are poured out into the canal, and act on the food-stuffs by dissolving some of them, and rendering others more or less soluble and diffusible. The **digested products pass into the blood**, either directly into the rootlets of the portal vein or indirectly by the lacteals. The small undigested part of the food is discharged in the fæces. The digested products thus finally reach the blood, so that in this way new matter is brought within the reach of the tissues. Stated broadly, then, the process of digestion consists in rendering **food-stuffs soluble and diffusible**, so that they can pass into the blood.]

141. THE MOUTH AND ITS GLANDS.—The **mucous membrane** of the cavity of the mouth, which becomes continuous with the skin at the red margin of the lips, has a number of **sebaceous glands** in the region of the red part of the lip. The buccal mucous membrane consists of bundles of fine fibrous tissue mixed with elastic fibres, which traverse it in every direction. **Papillæ**—simple or compound—occur near the free surfaces. The **sub-mucous tissue**, which is directly continuous with the fibrous tissue of the mucous membrane itself, is thickest where the mucous membrane is thickest, and densest where it is firmly fixed to the periosteum of the bone and to the gum; it is thinnest where the mucous membrane is most movable, and where there are most folds. The cavity of the mouth is lined by **stratified squamous epithelium**, which is thickest, as a rule, where the longest papillæ occur. [The mouth is formed by an involution of the external skin, and its epithelium is of epiblastic origin.]

All the **glands of the mouth**, including the salivary glands, may be divided into different classes according to the nature of their secretions.

1. The **serous** or **albuminous glands** [**true salivary**], whose secretion contains

a certain amount of albumin, *e.g.*, the human parotid. [The parotid of the cat, dog, rabbit, sub-maxillary of the rabbit and guinea-pig.]

2. The **mucous** glands, whose secretion, in addition to some albumin, contains the characteristic constituent mucin. [Sub-lingual of the rabbit, cat, dog, and sub-maxillary of the dog and cat.]

3. The **mixed** [or **muco-salivary**] glands, some of the acini secreting an albuminous fluid and others mucin, *e.g.*, the sub-maxillary and sub-lingual of man and ape.

Numerous **mucous glands** (labial, buccal, palatine, lingual, molar) have the appearance of small macroscopic bodies lying in the sub-mucosa. They are **branched tubular glands**, and the contents of their secretory cells consist partly of mucin, which is expelled from them during secretion. The excretory ducts of these glands, which are lined by cylindrical epithelium, are constricted where they enter the mouth. Not unfrequently one duct receives the secretion of a neighbouring gland.

The **glands of the tongue** form two groups, which differ morphologically and physiologically. (1) The **mucous glands** (**Weber's glands**), occurring chiefly near the root of the tongue, are branched tubular glands lined with clear transparent secretory cells whose nuclei are placed near the attached end of the cells. The acini have a distinct membrana propria. (2) The **serous glands**

(**Ebner's**) are acinous glands occurring in the region of the circumvallate papillæ (and in animals near the papillæ foliatae). They are lined with turbid granular epithelium with a central nucleus, and secrete saliva. (3) The **glands of Blandin and Nuhn** are placed near the tip of the tongue, and consist of mucous and serous acini, so that they are mixed glands (*Podwisotzky*).

The **blood-vessels** are moderately abundant, and the larger trunks lie in the sub-mucosa, whilst the finer twigs penetrate into the papillæ, where they form either a capillary network or simple loops.

The larger **lymphatics** lie in the sub-mucosa, whilst the finer branches form a fine network placed in the mucosa. The **lymph-follicles** also belong to the lymphatic system (§ 197). On the dorsum of the posterior part of the tongue they form an almost continuous layer. They are round or oval (1-1.5 mm. in diameter), lying in the sub-mucosa, and consist of adenoid tissue loaded with lymph-corpuscles. The outer part of the adenoid reticulum is compressed so as to form a kind of capsule for each follicle. Similar follicles occur in the intestine as solitary

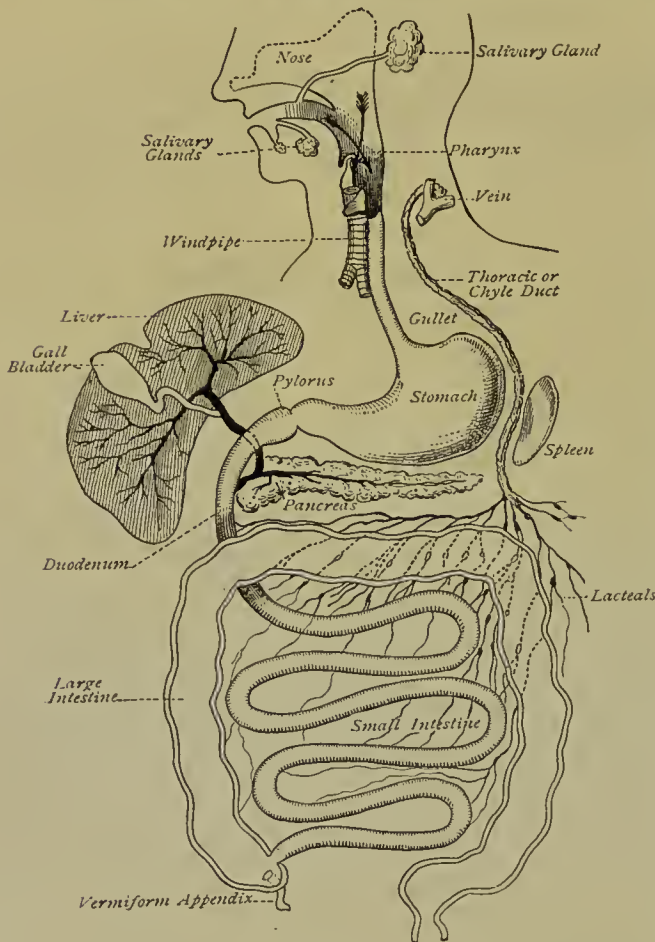


Fig. 172.

General scheme of the digestive tract, with the chief glands opening into it; together with the lacteals arising from the intestine and joining the thoracic duct.

follicles; in the small intestine they are collected together into Peyer's patches, and in the spleen they occur as Malpighian corpuscles. On the dorsum of the tongue several of these follicles form a slightly oval elevation, which is surrounded by connective-tissue. In the centre of this elevation there is a depression, into which a mucous gland opens, which fills the small crater with mucus (fig. 173).

The **tonsils** have fundamentally the same structure. On their surface are a number of depressions into which the ducts of small mucous glands open. These depressions are surrounded by groups (10-20) of lymph-follicles, and the whole is environed by a capsule of connective-tissue (fig. 174). Large lymph-spaces, communicating with lymphatics, occur in the neighbourhood of the tonsils, but as yet a direct connection between the spaces in the follicles and the lymph-vessels has not been proved to exist. Similar structures occur in the **tubal and pharyngeal tonsils**. [An enormous number of leucocytes wander out of the tonsils, solitary and Peyer's glands, and the adenoid tissue of the bronchial mucous membrane (fig. 174). The cells pass out between the epithelial cells, but do not pass into the interior of the latter (Stöhr).]

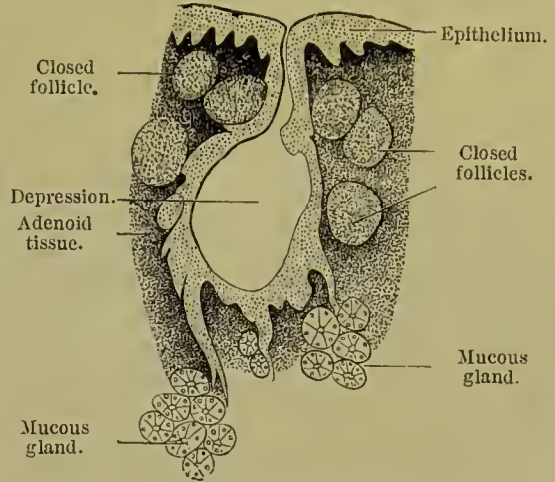


Fig. 173.

Section of a mucous follicle from the tongue.

[**Development of the Tonsil.**—The development of the palatal tonsil is most easily studied in the rabbit, where the single primary crypt generally remains without branches through life, and there the tonsil first appears in embryos $\frac{5}{8}$ of an inch long (occipito-sacral measurement), or

of about 12 days, as a shallow epithelial fold whose apex points directly backwards into the connective-tissue concentrically condensed round the pharynx. At this stage there is no infiltration of leucocytes in the connective-tissue round the crypt, and it is not until the embryos are about 21 days old ($1\frac{3}{4}$ inches long), that the leucocyte infiltration becomes evident. The crypt has then become much deeper and broader, and by its ingrowth has produced a condensation of the connective-tissues at right angles to the original peripharyngeal condensation as well as a great increase in the number of capillary blood-vessels. From this stage the elongation of the crypt, the condensation of the connective-tissue, the increase in the number of blood-vessels, and in the amount of leucocyte infiltration go on *pari passu*, until the adult condition is reached. As soon as the leucocytes appear in number in the submucous tissue they proceed to wander through the epithelium as Stöhr has described.

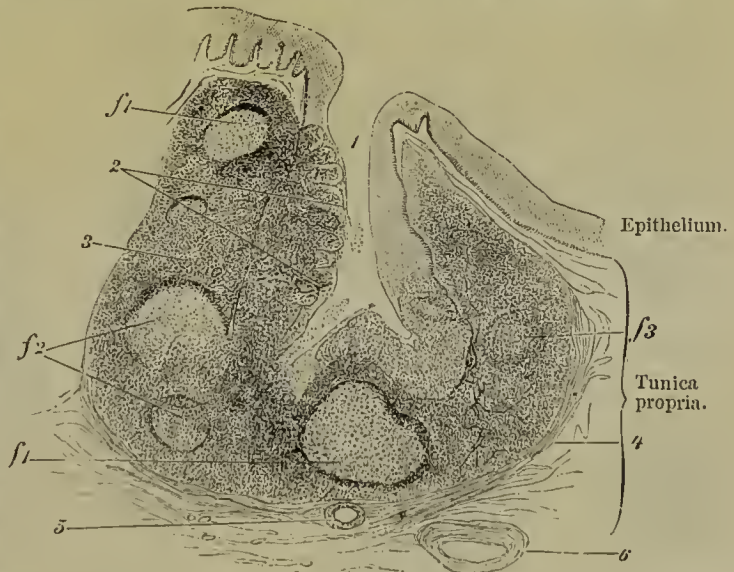


Fig. 174.

Vertical section of a human tonsil, $\times 20$. 1, cavity; 2, epithelium infiltrated with leucocytes below and on the left, but free on the right; 3, adenoid tissue with sections f_1 , f_2 , f_3 , of masses of it; 4, fibrous sheath; 5, section of a gland-duct; 6, blood-vessel.

In the fetus of the pig the condensation of the connective-tissue, especially at the apex of

the tonsillar crypts, and the consequent massing of leucocytes, mainly at these points, is particularly well shown.

In the human fœtus the process is the same, though complicated by the early ramification of the original epithelial crypt, and the appearance of fresh ones. The crypts become so deep that the cells from the surface layers of their epithelium cannot at once be thrown off into the mouth, and remain as a concentrically arranged mass of degenerated cornified cells filling up the lumen of the crypt; this mass is ultimately forced out by the *vis a tergo* of the leucocytes emigrating through the epithelium. (It will at once be seen how closely this resembles the formation of the concentric corpuscles of the thymus. The tonsils are preserved from the fate of the epithelial thymus by retaining their lumen.)

The prime factor in the formation of the tonsils is the epithelial ingrowth, which partly mechanically compresses the meshes of the connective-tissue, and partly causes proliferation of the connective cells and vessels by the slight irritation it produces, thereby making it easier for the leucocytes to escape from the thin-walled capillaries and veno-capillaries so formed, and, when they have escaped, causing them to be detained in the finely-meshed connective-tissue longer than in other situations. As the leucocytes are well supplied with nutriment, they divide by mitosis here in large numbers, as Flemming and his pupils first showed, and at a late stage in development (with great variations in individuals) "germ-centres" are formed, where a special arrangement of connective-tissue and vessels favours this process of division.

The lingual and pharyngeal tonsils develop in the same way as the palatal. His shows that all the tonsils arise behind the membrana pharyngis, and consequently, all these epithelial ingrowths pass into connective-tissue already condensed round the primitive alimentary canal (*G. L. Gulland*.)

Nerves.—Numerous *medullated* nerve-fibres occur in the sub-mucosa, pass into the mucosa, and terminate partly in the individual papillæ in Kranse's end-bulbs, which are most abundant in the lips and soft palate, and not so numerous in the cheeks and floor of the mouth. The nerves administer not only to common sensation, but they are also the organs of transmission for tactile (heat and pressure) impressions. It is highly probable, however, that some nerve-fibres end in fine terminal fibrils, between the epithelial cells, as in the cornea and elsewhere.

[**Secretory glands** may be **simple** or **compound**. In the latter case the duct is branched. In the course of **development**, a solid process of the epithelium sinks

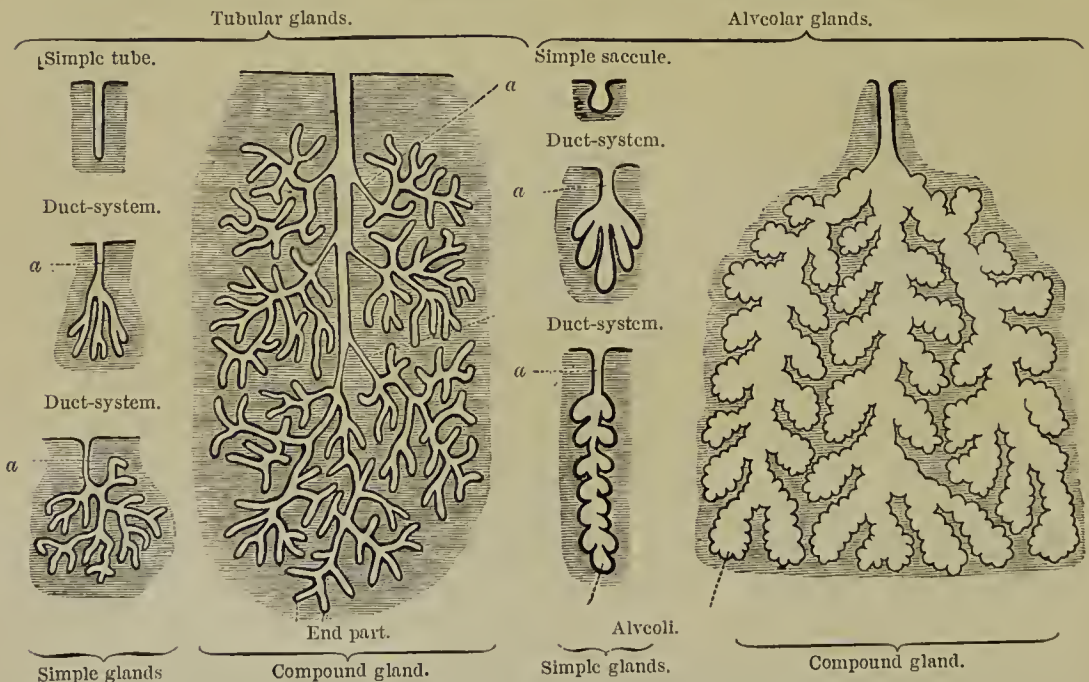


Fig. 175.

Scheme of different forms of gland; α , duct.

into the subjacent fibrous tissue, and, to form a simple gland, a cavity appears in this bud, but for a compound gland, other epithelial buds sprout from its blind end. Each bud acquires a central cavity; these elongate and increase in

number, thus forming a much-branched system, the terminal blind ends forming the **acini**, **alveoli**, or true secretory part. If the alveoli are tubular in shape, the gland is called a compound tubular gland. Thus in the compound glands some parts are secretory, and others act as ducts, while in the simple glands all the parts may be secretory. All the glands opening on the surface of the body are of epiblastic origin. The secretory cells lining the acini rest on a basement membrane, and outside this are the lymph-spaces and capillary blood-vessels.]

[Flemming has recently proposed a new classification of glands. Glands are developed from the epithelium of mucous membranes, and that of the skin. They are therefore hollow inflections of the surface epithelium into the subjacent connective-tissue, and may be either cylindrical tubes—**tubuli**—or with dilatations or sacculations, **alveoli**—so that two chief kinds are distinguished—**tubular** and **alveolar glands** (fig. 175).

I. **Tubular glands** occur either singly, or arranged in groups, so that they are divided into—
1. **Simple tubular glands**, which are either simple or branched tubes leading to a duct (fig. 175). The latter form has been called a “duct-system.”

2. **Compound tubular glands**, composed of a number of “duct-systems” (fig. 175).

II. **Alveolar glands** are similarly classified.

1. **Simple alveolar glands**, with either a simple or branched dilatation or sacculus communicating with a duct; the latter is called an “alveolar system.”

2. **Compound alveolar glands**, which consist of several alveolar systems.

Unbranched simple tubular glands are: Lieberkühn's glands, sweat-glands, and the glands of the fundus of the stomach.

Branched tubular simple glands are: the pyloric, Brunner's, the smallest mucous and serous glands of the mouth, and the uterine glands.

Compound tubular glands are: the larger mucous, and salivary and lachrymal glands. Also the kidneys, Cowper's glands, prostatic glands, thyroid (at an early stage), liver, and testis. The branches of the latter two glands anastomose and form a network; hence the liver and testis have been called “reticular glands.”

Unbranched simple alveolar glands are: the smallest sebaceous glands and the ovarian follicles.

Branched alveolar simple glands are: the larger sebaceous glands and the Meibomian glands.

Compound alveolar glands are: the mammary glands and the lungs (Flemming and Stöhr).]

142. THE SALIVARY GLANDS.—There are **three pairs** of salivary glands, **sub-maxillary**, **sub-lingual**, and **parotid**. [The **sub-maxillary gland** lies under



Fig. 176.

A, duct and acini of the parotid gland of a dog; B, acini of the sub-maxillary gland of a dog; c, refractive mucous cells; d, granular half-moons of Giannuzzi; C, similar alveoli after prolonged secretion; D, basket-shaped tissue investment of an acinus; F, entrance of a non-medullated nerve-fibre into a secretory cell.

the horizontal ramus of the lower jaw, and its duct (50 mm. long)—the **duct of Wharton**—opens in the floor of the mouth at the side of the frænum of the tongue.

The **parotid**, the largest of the glands, lies close to the auricle, and its duct—the **duct of Steno**—passes over the masseter muscle, perforates the buccinator muscle obliquely, and opens into the mouth opposite the second upper molar tooth. The **sub-lingual gland** is the smallest of the three, lies beneath the tongue, and has a number of small ducts (10–20)—the **ducts of Rivini**—some of which open separately, but one larger one—the **duct of Bartholin**—unites with Wharton's duct. All these glands are **compound tubular glands**.] [Each gland consists of a number of lobes, and each lobe in turn of a number of lobules, which, again, are

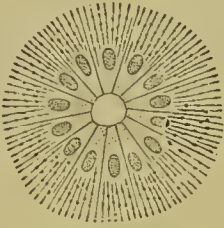


Fig. 177.

Rodded epithelium lining the duct of a salivary gland.

composed of **acini**. All these are held together by a **framework** of connective-tissue. The larger branches of the **duct** lie between the lobules, and constitute the **interlobular** ducts, giving branches to each lobule which they enter, constituting the **intralobular** ducts, which branch and finally terminate in connection with the alveoli, by means of an **intermediary** or **intercalary part** or **ductule**. The larger interlobar and interlobular ducts consist of a membrana propria, strengthened outside by fibrous and elastic tissue, and in some places also by non-striped muscle, while the ducts are lined by columnar epithelial cells. In the largest branches there

is a second row of smaller cells, lying between the large cells and the membrana propria. The **intralobular ducts** are lined by a single layer of large cylindrical epithelium with the nucleus about the middle of the cell, while the outer half of the cell is finely striated longitudinally, or "**rodde**d," which is due to fibrillæ

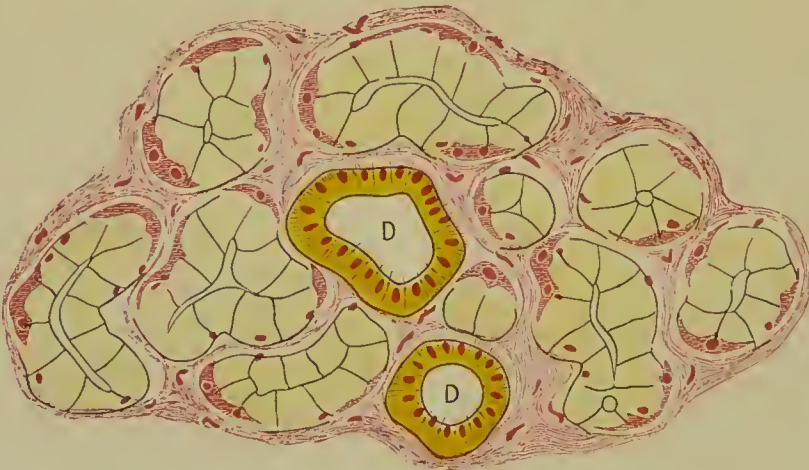


Fig. 178.

Section of the sub-maxillary gland of the dog stained with picro-carmine; D, duct.

(fig. 177); the inner half next the lumen is granular. The **intermediary part** is narrow, and is lined by a single layer of flattened cells, each with an elongated oval nucleus. There is usually a narrow "neck," where the intralobular duct becomes continuous with the intermediary part, and here the cells are polyhedral.]

The **terminal acini**, or **alveoli**, are the parts where the actual process of secretion takes place. Fig. 176, A, shows several ducts terminating in acini. The acini vary somewhat in shape—some are tubular, others branched, some are dilated and resemble a Florence flask, and several of them usually open into one intermediary part of a duct. Each alveolus is bounded by a basement membrane, with

a reticulate structure made up of nucleated, branched, and anastomosing cells so as to resemble a basket (I). There is a homogeneous membrane bounding the alveoli in addition to this basket-shaped structure. Immediately outside this membrane is a lymph-space, and outside this again the network of capillaries is distributed. [The extent to which this lymph-space is filled with lymph determines the distance of the capillaries from the membrana propria. The interalveolar lymph-spaces communicate with large lymph-spaces between the lobules, which in turn communicate with perivascular lymphatics around the arteries and veins.] The lymphatics emerge from the gland at the hilum.

The **secretory cells** vary in structure, according as the salivary gland is a **mucous** [sub-maxillary and sub-lingual of the dog and cat], a **serous** [parotid of man and mammals, and sub-maxillary of rabbit], or a **mixed gland** [human sub-maxillary and sub-lingual].

Mucous Acini.—The secretory cells of mucous glands, and the mucous acini of mixed glands (figs. 178, 179) are lined by a single layer of "**mucin cells**" (fig. 176, B, c), which are large cells distended with mucin, or with a hypothetical substance, **mucigen**, which yields mucin. The mucin cells are more or less spheroidal in shape, clear, shining, highly refractive, and nearly fill the acinus. The flattened nucleus is near the wall of the acinus. Each cell has a fine process which overlaps the fixed parts of the cells next to it. Owing to the body of each cell being infiltrated with mucin, these cells do not stain with carmine, although the nucleus and its immediately investing protoplasm do. Another kind of cell occurs in the sub-maxillary gland of the dog. It forms a half-moon-shaped *structure* lying in direct contact with the wall of the acinus (*Gianuzzi*). Each "**demilune**" "**half-moon**," or "**crescent**" consists of a number of small closely packed, angular, highly albuminous cells with small oval nuclei, which, however, are separated only with difficulty. Hence, Heidenhain has called them "**composite marginal cells**" (B, d). They are granular, darker, devoid of mucin, and stain readily with pigments. [In the sub-maxillary gland of the cat, there is a complete layer of these "**marginal**" carmine-staining cells lying between the mucous cells and the membrana propria.]

[**Serous Acini.**—In true serous glands (parotid of man and mammals) and in the

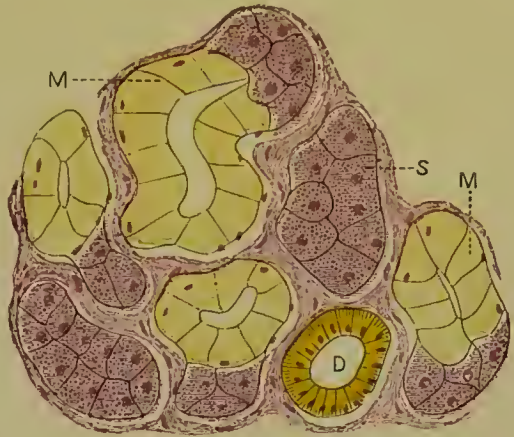


Fig. 179.

Section of retro-lingual gland of dog—a mixed gland—stained with picro-carmine. M, mixed acinus; S, serous acinus; D, duct.

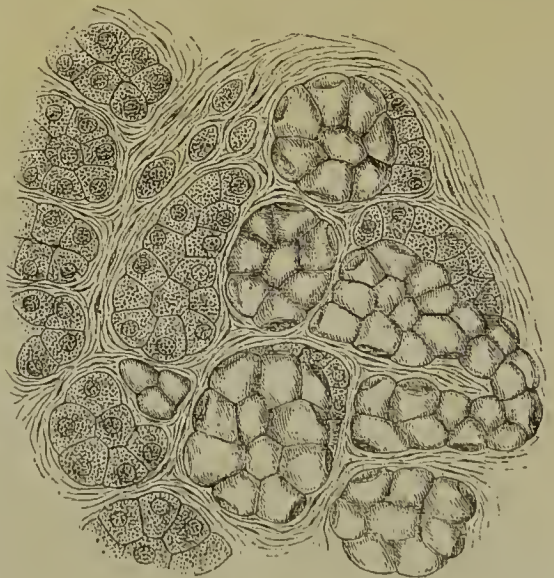


Fig. 180.

Section of a human sub-maxillary gland. On the left is a group of serous alveoli, and on the right a group of mucous alveoli.

serous acini of mixed glands, the acini are lined by a single layer of secretory columnar finely-granular cells, which in the quiescent condition completely fill the acinus, so that scarcely any lumen is left (fig. 176, C). Just before secretion, or when these cells are quiescent, Langley has shown that they are large and filled with numerous granules, which obscure the presence of the nucleus. As secretion takes place, these granules seem to be used up or discharged into the lumen; at least, the outer part of each cell gradually becomes clear and more transparent, and this condition spreads towards the inner part of the cell.]

[In the **mixed** or **muco-salivary** glands (*e.g.*, human sub-maxillary) some of the alveoli are mucous and others serous in their characters, but the latter are always far more numerous, and the one kind of acinus is directly continuous with the other kind (fig. 180).]

143. HISTOLOGICAL CHANGES DURING THE ACTIVITY OF THE SALIVARY GLANDS.—[The condition of physiological activity of the gland-cells is accompanied by changes in the histological characters of the secretory cells. Changes in **serous glands** have been carefully studied in the parotid of the rabbit, but the appearances vary somewhat, according as the glands are examined in the fresh condition or after hardening in various reagents, such as absolute alcohol. When the gland is at **rest**, or in the "**resting phase**," sometimes also called the "**loaded**" or "**charged**" condition, in a preparation hardened in alcohol, and stained with carmine, the cells consist of a pale, almost uncoloured substance, with a few fine granules, and a small irregular, red-stained, shrivelled nucleus devoid of a nucleolus. The appearance of the nucleus suggests the idea of its being shrivelled by the action of the hardening reagent (fig. 181, A).]

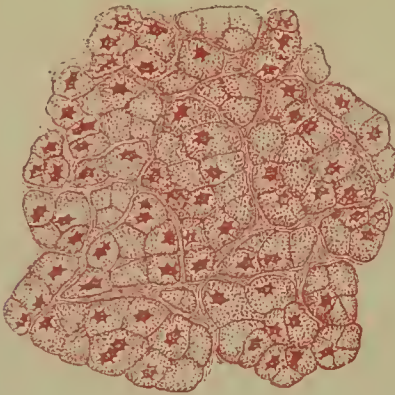


Fig. 181, A.

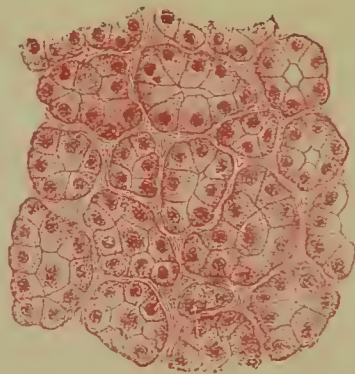


Fig. 181, B.

Sections of a "serous" gland, stained with carmine. The parotid of a rabbit, fig. 181, A, at rest; fig. 181, B, after stimulation of the cervical sympathetic.

[During activity, or in the "**active phase**," if the gland be caused to secrete by stimulating the sympathetic, all parts of the cells undergo a change (fig. 181, A, B). In preparations **hardened in alcohol**—(1) the cells diminish somewhat in size; (2) the nuclei are no longer irregular, but round, with a sharp contour and nucleoli; (3) the substance of the cell itself is turbid owing to the diminution of the clear substance, and the increase of the granules, especially near the nuclei; (4) at the same time, the whole cell stains more deeply with carmine (*Heidenhain*).]

[On studying the changes which occur in a **living serous gland**, Langley found that the substance of the cells of the parotid is pervaded by fine granules, which are so numerous as to obscure the nucleus, while the outlines of the cells are indis-

tinged. No lumen is visible in the acini, during **activity** the granules disappear from the outer zone of the cells, the cells themselves becoming smaller and more distinct. After prolonged secretion, the granules largely disappear from the cell-substance except quite near the inner margin. The cells are smaller, their outlines more distinct, their spherical nuclei apparent, and the lumen of the acini is wide and distinct. Thus, it is evident that, during rest, granules are manufactured, which disappear during the activity of the cells, the disappearance taking place from without inwards. Similar changes occur in the cells of the pancreas (§ 168).]

[More complex changes occur in the **mucous glands**, such as the sub-maxillary or orbital glands of the dog (*Lavdovsky*). The appearances vary according to the intensity and duration of the secretory activity. The mucous cells at **rest** are large, clear, and refractive, containing a flattened nucleus (fig. 176, C), surrounded with a small amount of protoplasm, and placed near the basement membrane. The clear substance does not stain with carmine, and consists of mucigen lying in the wide spaces of an intracellular plexus of fibrils. After **prolonged secretion**, produced, it may be, by strong and continued stimulation of the chorda, the mucous cells of the sub-maxillary gland of the dog undergo a great change. In such a condition the cells are spoken of as “unloaded” or “discharged.”] The distended, refractive, and “mucous cells,” which occur in the quiescent gland, and which do not stain with carmine, appear quite different after the gland has been in a state of activity. They are represented by small dark protoplasmic cells devoid of mucin (fig. 176, C). These cells readily stain with carmine, whilst their nucleus is scarcely, if at all, coloured by the dye. The researches of R. Heidenhain (1868) have shed much light on the secretory activity of these glands.

[During rest, the protoplasm seems to manufacture **mucigen**, which is changed into and discharged as mucin in the secretion, when the gland is actively secreting. Thus, the cells become smaller, but the protoplasm of the cell seems to increase, new mucigen is manufactured during rest, and the cycle is repeated.]

The change may be produced in two ways. Either it is due to the “mucous cells” during secretion becoming broken up, so that they yield their mucin directly to the saliva; in saliva rich in mucin, small microscopic pieces of mucin are found, and sometimes mucous cells themselves are present. Or, we must assume that the mucous cells simply eliminate the mucin from their bodies (*Ewald, Stöhr*); while after a period of rest, new mucin is formed. According to this view, the dark granular cells of the glands, after active secretion, are simply mucous cells, which have given out their mucin. If we assume, with Heidenhain, that the mucous cells break up, then these granular non-mucous cells must be regarded as new formations produced by the proliferation and growth of the composite marginal cells, *i.e.*, the crescents, or half-moons of Giannuzzi.

144. THE NERVES OF THE SALIVARY GLANDS.—The nerves are for the most part medullated, and enter at the hilum of the gland, where they form a rich plexus provided with **ganglia** between the lobules. [There are no ganglia in the parotid gland (*Klein*).]

All the salivary glands are supplied by branches from two different nerves—from the sympathetic and from a cranial nerve.

1. The **sympathetic nerve** gives branches (*a*) to the sub-maxillary and the sub-lingual glands, derived from the plexus on the external maxillary artery; (*b*) to the parotid gland from the carotid plexus (fig. 182). [These nerve-fibres reach the gland along the arteries of the gland, and are for the most part non-medullated nerve-fibres. They can be traced to the superior cervical ganglion and from thence through the cervical sympathetic into the cord.]

2. The **facial nerve** gives branches to the sub-maxillary and sub-lingual glands from the **chorda tympani**, which accompanies the lingual branch of the fifth nerve (fig. 182). [The chorda consists of fine medullated fibres, but as they enter the gland the fibres become non-medullated.] The branches to the parotid arise from the tympanic branch of the **glosso-pharyngeal nerve** (dog). The tympanic

plexus sends fibres to the small superficial petrosal nerve, and with it these fibres run to the anterior surface of the pyramid in the temporal bone, emerging from the skull through a fissure between the petrous and great wing of the sphenoid, and then joining the otic ganglion. This ganglion sends branches to the auriculo-temporal nerve (itself derived from the third branch of the trigeminus), which, as it passes upwards to the temporal region under cover of the parotid, gives branches to this gland.

The **sub-maxillary ganglion**, which gives branches to the sub-maxillary and

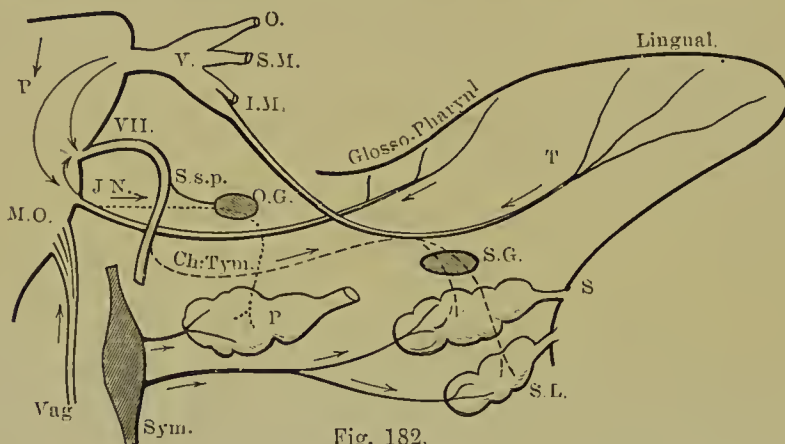


Fig. 182.

Scheme of the nerves of the salivary glands. P., pons; M.O., medulla oblongata; J.N., nerve of Jacobson; O., S.M., I.M., ophthalmic, superior, and inferior maxillary divisions of fifth nerve, V.; VII., seventh nerve; S.s.p., small superficial petrosal nerve; Vag., vagus; Sym., sympathetic; O.G., otic, and S.G., sub-maxillary ganglia; P., S., and S.L., parotid, sub-maxillary, and sub-lingual glands; T., tongue.

sub-lingual glands, receives fibres from the tympanico-lingual nerve (chorda tympani) as well as sympathetic fibres from the plexus on the external maxillary artery.

Termination of the Nerve-Fibres.—With regard to the ultimate distribution of these nerves we can distinguish (1) the **vaso-motor nerves**, which give branches to the walls of the blood-vessels, and (2) the **secretory nerves** proper.

Pflüger states, with regard to the latter, that (a) medullated nerve-fibres penetrate the acini; the sheath of Schwann unites with the membrana propria of the acinus; the medullated fibre—still medullated—passes between the secretory cells, where it divides and becomes non-medullated, and its axial cylinder terminates in connection with the nucleus of a secretory cell. [This, however, is not proved] (fig. 176, F). (b) According to Pflüger, some of the nerve-fibres end in multipolar ganglion cells, which lie outside the wall of the acinus, and these cells send branches to the secretory cells of the acini. [These cells probably correspond to the branched cells of the basket-shaped structure.] (c) Again, he describes medullated fibres which enter the attached end of the cylindrical epithelium lining the excretory ducts of the glands (E). Pflüger thinks that those fibres entering the acini directly are cerebral, while those with ganglia in their course are derived from the sympathetic system. [(d) The direct termination of nerve-fibres has been observed in the salivary glands of the cockroach by Kupffer.]

145. ACTION OF THE NERVOUS SYSTEM ON THE SECRETION OF SALIVA.—A. **Sub-maxillary Gland.**—Stimulation of the facial nerve at its origin causes a profuse secretion of a thin **watery saliva**, which contains a very small amount of specific constituents. Simultaneously with the act of secretion, the blood-vessels of the glands dilate, and the capillaries are so distended that the pulsatile movement in the arteries is propagated into the veins. [Owing to the dilatation of the arterioles the pulse-wave is propagated through the capillaries into the veins, so that there is a venous pulse, the blood flowing from the veins in jets, p. 135.] Nearly four times as much blood flows out of the veins, the

blood being of a bright red colour, and containing one-third more O than the venous blood of the non-stimulated gland. Notwithstanding this relatively high percentage of O, the secreting gland uses more O than the passive gland (§ 131, 1).

[I. **Stimulation of Chorda Tympani.**—If a cannula be placed in Wharton's duct, *e.g.*, in a dog, and the chorda tympani be divided, no secretion flows from the cannula. On stimulating the *peripheral end of the chorda tympani* with an interrupted current of electricity, the same results—copious secretion of saliva and vascular dilatation, with increased flow of blood through the gland—occur as when the origin of the seventh nerve itself is stimulated.—The **watery** saliva is called **chorda saliva**. Thus two effects are produced simultaneously, *viz.*, **vascular dilatation** and **secretion of saliva**. As a matter of fact, each is brought about by the independent action of special nerve-fibres, so that two functionally different kinds of nerve-fibres occur in the facial nerve and chorda—(1) **vaso-dilator fibres** (fig. 183), and (2) true **secretory fibres**. The methods by which the existence of these nerve-fibres is proved are described on p. 248].

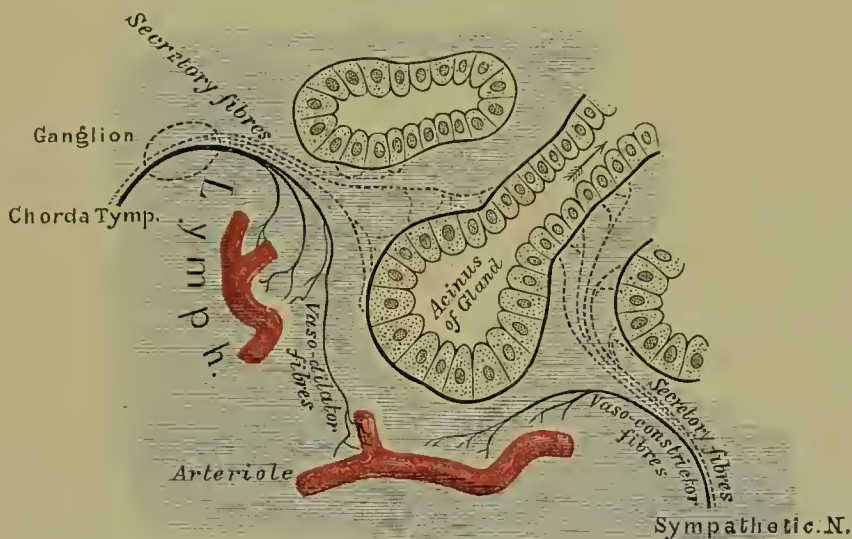


Fig. 183.

Scheme of the secretory and vaso-constrictor nerves of the sympathetic nerve, and vaso-dilator and secretory nerves of the chorda passing to the sub-maxillary gland.

II. **Stimulation of the sympathetic nerve** causes a scanty amount of a very **thick**, sticky, opaque mucous secretion, in which the specific salivary constituents, *mucin*, and the salivary corpuscles are very abundant. [It contains a large number of morphological elements, chiefly pale glutinous-looking masses, probably products of the transformation of gland-cells. The solids reach 15–28 per 1000, but the total quantity of saliva secreted is always small.] The specific gravity of the saliva is raised from 1007 to 1010. Simultaneously the blood-vessels become contracted, so that the blood flows more slowly from the veins, and has a dark bluish colour.

The sympathetic also contains *two* kinds of nerve-fibres—(1) true **secretory fibres**, and (2) **vaso-constrictor fibres** (fig. 183).

[**Electrical Variations during Secretion.**—That changes in the electromotive properties of glands occur during secretion was shown in the frog's skin. Bayliss and Bradford find that the same is true of the sub-maxillary gland (dog). During secretion, the **excitatory** change on stimulating the **chorda** is a *positive* variation of the current of rest (the hilum of the gland becoming more positive), but it is frequently followed by a second phase of opposite sign. The latent period is always very short, about 0·37". Atropin abolishes the chorda variation. On

stimulating the sympathetic, the excitatory change is of an opposite sign to that of the chorda, and the hilum becomes less positive, so that there is a *negative* variation. It requires a more powerful stimulus, is less in amount, and its latent period is longer (2"-4"), while atropin lessens but does not abolish it.]

Relation to Stimulus.—On stimulating the cerebral nerves, at first with a weak and gradually with a stronger stimulus, there is a gradual development of the secretion in which the solid constituents—occasionally the organic—are increased (*Heidenhain*). If a strong stimulus be applied for a long time, the secretion diminishes, becomes watery, and is poor in specific constituents, especially in the organic elements, which are more affected than the inorganic (*C. Ludwig and Becher*). After prolonged stimulation of the sympathetic, the secretion resembles the chorda saliva. It would seem, therefore, that the chorda and sympathetic saliva are not specifically distinct, but vary only in degree. On continuing the stimulation of the nerves up to a certain maximal limit, the rapidity of secretion becomes greater, and the percentage of salts also increases to a certain maximum, and this independently of the former condition of the glands. The percentage of organic constituents also depends on the strength of the nervous stimulation, but not on this alone, as it is essentially contingent upon the condition of the gland before the secretion took place, and it also depends upon the duration and intensity of the previous secretory activity. Very strong stimulation of the gland leaves an "after effect," which predisposes it to give off organic constituents into the secretion (*Heidenhain*). A latent period of 1.2 sec. to 24 sec. may elapse between the nerve-stimulation and the beginning of the secretion.

[Langley has shown that in the cat the sympathetic saliva of the sub-maxillary gland is less viscid than the chorda saliva.]

Relation of Secretion to Blood-Supply.—*The secretion of saliva is not simply the result of the amount of blood in the glands; that there is a factor independent of the changes in the state of the vessels is shown by the following facts:—*

1. The secretory activity of the glands when their nerves are stimulated continues for some time after the blood-vessels of the gland have been ligatured.

[If the head of a rabbit be cut off, stimulation of the seventh nerve, above where the chorda leaves it, causes a flow of saliva, which cannot be accounted for on the supposition that the saliva already present in the salivary glands is forced out of them. Thus we may have secretion without a blood-stream. The saliva is really secreted from the lymph (fig. 183) present in the lymph-spaces of the gland (*Ludwig*).]

2. Atropin and daturin abolish the activity of the secretory fibres in the chorda tympani, but do not affect the vaso-dilator fibres (*Heidenhain*). The same results occur after the injection of acids and alkalies into the excretory duct (*Gianuzzi*).

[**Action of Atropin.**—The vascular dilatation and the increased flow of saliva due to the activity of the secretory cells, produced by stimulation of the chorda tympani, although they occur simultaneously, do not stand in the relation of cause and effect. We may cause vascular dilatation without an increased flow of saliva, as already stated (2). If atropin be given to an animal, stimulation of the chorda produces dilatation of the blood-vessels, but no secretion of saliva. Atropin paralyses the secretory fibres, but not the vaso-dilator fibres (fig. 184). The increased supply of blood, while not causing, yet favours the act of secretion, by placing a large amount of pabulum at the disposal of the secretory elements, the cells.]

3. The pressure in the excretory duct of the salivary gland—measured by means of a manometer tied in it—may be nearly twice as great as the pressure within the arteries of the glands, or even in the carotid itself (*Ludwig*). The pressure in Wharton's duct may reach 200 mm. Hg [while the pressure within the carotid, *i.e.*, the blood-pressure, may be only 120 mm. Hg.]

[**Secretory Pressure.**—The experiment described under (3) proves, in a definite manner, that the passage of the water from the blood-vessels, or at least from the lymph into the acini of the gland, cannot be due to the blood-pressure; that, in fact, it is not a mere process of filtration, such as perhaps occurs in the glomeruli of the kidney. In the case of the salivary gland, where the pressure within the gland may be nearly double that of the arterial pressure, the water actually moves from the lymph-spaces against very great resistance. We can only account for

this result by ascribing it to the secretory activity of the gland-cells themselves. Whether the activities of the gland-cells, as suggested by Heidenhain, are governed directly by two distinct kinds of nerve-fibres, a set of solid-secreting fibres, and a set of water-secreting fibres, remains to be proved.]

All these facts lead us to conclude that **the nerves exercise a direct effect upon the secretory cells**, apart from their action on the blood-vessels.

4. Just as in the case of muscles and nerves, the salivary glands become **fatigued** or exhausted after prolonged action. This result may also be brought about by injecting acids or alkalis into the duct, which shows that the secretory activity of the gland is independent of the circulation (*Gianuzzi*).

Extirpation of Salivary Glands.—When the chorda tympani is extirpated on one side in young dogs, the sub-maxillary gland on that side does not develop so much—its weight is 50 per cent. less—while the mucous cells and the “crescents” are smaller than on the sound side (*Bufalini*).

During secretion, the **temperature** of the gland rises 1.5° C. (*Ludwig*), and the blood flowing from the veins is often warmer than the arterial blood. [The **electromotive changes** are referred to at p. 247.]

[**Results of Stimulation of glandular nerves.**—The results following electrical or other stimulation of the peripheral end of a glandular nerve may be stated as follows:—

(1) **Vaso-motor changes**, causing alterations in the blood-supply and blood-flow.

(2) **Chemical and histological changes** in the gland-cells connected with the elaboration of the organic and possibly of the inorganic constituents of the saliva.

(3) Changes by which **water is secreted**, *i.e.*, passes through the basement membrane and gland-cells, and the consequent movement of the fluid through the cells and ducts.

(4) **Electrical changes** (p. 247), which do not seem to be associated with the vaso-motor changes, for the electrical variations are readily abolished by atropin, which does not affect the vaso-motor changes.]

“Paralytic Secretion” of Saliva.—By this term is meant the continued secretion of a thin watery saliva from the sub-maxillary gland, which occurs twenty-four hours after the section of the *cerebral nerves* (chorda of the seventh), *i.e.*, those branches of them that go to this gland, whether the sympathetic be divided or not (*Cl. Bernard*). It increases until the eighth day, after which it gradually diminishes, while the **gland-tissue degenerates**. The injection of a small quantity of curare into the artery of the gland also causes it.

[Heidenhain showed that section of *one* chorda is followed by a continuous secretion of saliva from *both* sub-maxillary glands. The term “**paralytic secretion**” is applied to that which takes place on the side on which the nerve is cut, and Langley proposes to call the secretion on the opposite side the **antilytic**. Apnoea (§ 368) stops both the paralytic and antilytic secretion, while dyspnoea increases the flow in both cases; and as section of the sympathetic fibres to the gland (where the chorda is cut) arrests the paralytic secretion excited by dyspnoea, it is evident that both the paralytic secretion and the secretion following dyspnoea are caused by stimuli travelling down the sympathetic fibres. In the later stages of the paralytic secretion the cause is in the gland itself, for it goes on even if all the nerves passing to the gland be divided, and is probably due to a local nerve-centre. In this stage the secretion is arrested by a large dose of chloroform. The paralytic secretion, in the first stage, may be owing to a venous condition of the blood acting on a central secretory centre whose excitability is increased; and in the latter stages probably on local nerve-centres within the gland. The fibres of the chorda in the cat are only partially degenerated thirteen days after section (*Langley*).]

[**Histological Changes.**—In the gland during paralytic secretion, the gland-cells of the alveoli (serous, mucous, and demilunes) diminish in size, and show the typical “resting” appearance, even to a greater extent than the normal resting gland (*Langley*).]

B. Sub-Lingual Gland.—Very probably the same general relations obtain as in the sub-maxillary gland.

C. Parotid Gland.—In the dog, stimulation of the sympathetic *alone* causes no

secretion ; it occurs when the glosso-pharyngeal branch to the parotid is simultaneously excited. This branch may be reached within the tympanum in the tympanic plexus. A *thick* secretion containing much organic matter is thereby obtained. Stimulation of the *cerebral* branch *alone* yields a clear thin watery secretion, containing a very small amount of organic substances, but a considerable amount of the salts of the saliva.

[Stimulation of Jacobson's Nerve (Parotid of Dog)—

	Total Solids.	Salts.	Organic Matter.
Without sympathetic, ...	0·55%	0·31	0·24
With sympathetic, ...	2·42%	0·36	2·06]

The following table shows the nerves of the parotid gland :—

<i>Vaso-motor nerves</i>	{ Cerebral. Vaso dilators = glosso-pharyngeal. Sympathetic. Vaso-constrictors = sympathetic.
<i>Secretory nerves</i>	{ Cerebral { Faical (?) { Glosso-pharyngeal } = small superficial petrosal. { Sympathetic = sympathetic.]

The parotid atrophies after destruction of the tympanic plexus (*Bradford*).

Reflex Secretion of Saliva.—[If a cannula be placed in Wharton's duct, *e.g.*, in a dog, during fasting, little or no saliva will flow out, but on applying a sapid substance to the mucous membrane of the mouth or the tongue, there is a copious flow of saliva. If the sympathetic nerve be divided, secretion still takes place when the mouth is stimulated, but if the chorda tympani be cut, secretion no longer takes place. Hence, the secretion is due to a reflex act ; in this case, the lingual is the afferent, and the chorda the efferent nerve carrying impulses from a centre situated in the medulla oblongata (fig. 184).] In the intact body, the

secretion of saliva occurs through a **reflex** stimulation of the nerves concerned, whereby, under normal circumstances, the secretion is always watery (chorda or facial saliva). The **centripetal** or **afferent nerve-fibres** concerned are :—(1) The nerves of taste. (2) The sensory branches of the trigemini of the entire cavity of the mouth and the glosso-pharyngeal (which appear to be capable of being stimulated by mechanical stimuli, pressure, tension, displacement). The movements of mastication also cause a secretion of saliva. Pflüger found that one-third more saliva was secreted on the side where mastication took place ; and Cl. Bernard observed that the

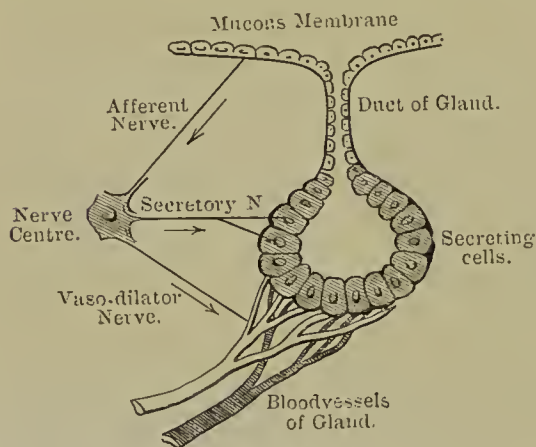


Fig. 184.

Diagram of a salivary gland.

secretion ceased in horses during the act of drinking. (3) The nerves of smell, excited by certain odours. (4) The gastric branches of the vagus. A rush of saliva into the mouth usually precedes the act of vomiting (§ 158).

(5) The stimulation of distant sensory nerves, *e.g.*, the central end of the sciatic—certainly through a complicated reflex mechanism—causes a secretion of saliva (*Oresjannikow and Tschierjew*). Stimulation of the conjunctiva, *e.g.*, by applying an irritating fluid to the eye of carnivorous animals, causes a reflex secretion of saliva (*Aschenbrandt*). Perhaps the secretion of saliva which sometimes occurs during pregnancy is caused in a similar reflex manner.

(6) The movements of mastication excite secretion, but although, during the act of rumination, this is the case in ruminants, in whom the process of mastication is very thorough, there is no secretion from the sub-maxillary gland, although the parotid secretes (*Colin, Ellenberger and Hofmeister*).

The **reflex centre** for the secretion of saliva lies in the medulla oblongata, at the origin of the seventh and ninth cranial nerves. The centre for the sympathetic fibres is also placed here. This region is connected by nerve-fibres with the cerebrum; hence the thought of a savoury morsel, sometimes, when one is hungry, causes a rapid secretion of a thin watery fluid—[or, as we say, “makes the mouth water”]. If the centre be stimulated directly by a mechanical stimulus (puncture), salivation occurs, while asphyxia has the same effect. The reflex secretion of saliva may be **inhibited** by stimulation of certain sensory nerves, *e.g.*, by pulling out a loop of the intestine. Stimulation of the cortex cerebri of a dog, near the sulcus cruciatus, is often followed by secretion of saliva. Disease of the brain in man sometimes causes a secretion of saliva, owing to the effects produced on the intracranial centre.

So long as there is no stimulation of the nerves, there is no secretion of saliva, as in sleep. *Immediately after* the section of all nerves, secretion stops, for a time at least.

Pathological Conditions and Poisons.—Certain affections, as inflammation of the mouth, neuralgia; ulcers of the mucous membrane; and affections of the gums, due to teething or the prolonged administration of mercury, often produce a copious secretion of saliva or **ptyalism**. Certain **poisons** cause the same effect by direct stimulation of the nerves, as Calabar bean (physostigmin), digitalin, and especially pilocarpin. Many poisons, especially the narcotics—above all **atropin**—*paralyse the secretory nerves*, so that there is a cessation of the secretion and the mouth becomes dry; while the administration of muscarin in this condition causes secretion. Pilocarpin acts on the chorda tympani, causing a profuse secretion, and if atropin be given, the secretion is again arrested. Conversely, if the secretion be arrested by atropin, it may be restored by the action of pilocarpin or physostigmin. Nicotin, in small doses, excites the secretory nerves, but in large doses paralyzes them. Daturin, cicutin, and iodide of æthylstrychnin, paralyse the chorda. The saliva is diminished in amount in man, in cases of *paralysis of the facial* or sympathetic nerves, as is observed in unilateral paralysis of these nerves.

[**Sialogogues** are those drugs which increase the secretion of saliva. Some are **topical**, and take effect when applied to the mouth. They excite secretion reflexly by acting on the sensory nerves of the mouth. They include acids, and various pungent bodies, such as mustard, ginger, pyrethrum, tobacco, ether, and chloroform; but they do not all produce the same effect on the amount or quality of the saliva; others, the **general sialogogues**, cause salivation when introduced into the blood: physostigmin, nicotin, pilocarpin, muscarin. The drugs named act after all the nerves going to the gland are divided, so that they stimulate the peripheral ends of the nerves in the glands. The first two also excite the central ends of the secretory nerves.]

[**Anti-sialics** are those substances which diminish the secretion of saliva, and they may take effect upon any part of the reflex arc, *i.e.*, on the mouth, the afferent nerves, the nerve-centre and afferent nerves, or upon the blood-stream through the glands, or in the glands themselves. Opium and morphia affect the centre, large doses of physostigmin affect the blood-supply, but atropin is the most powerful of all, as it paralyzes the terminations of the secretory nerves in the glands, *e.g.*, the chorda tympani, and even the sympathetic in the cat (but not in the dog).]

[**Excretion by the saliva.**—Some drugs are excreted by the saliva. Iodide of potassium is rapidly eliminated by the kidneys, and by the salivary glands, and so also is iodide of iron.]

Theory of Salivary Secretion.—Heidenhain has recently formulated the following theory regarding the secretion of saliva:—“During the passive or quiescent condition of the gland, the organic materials of the secretion are formed from and by the activity of the protoplasm of the secretory cells. A *quiescent* cell, which has been inactive for some time, therefore contains little protoplasm, and a large amount of these secretory substances. In an actively secreting gland, there are two processes occurring together, but independent of each other, and regulated by two different classes of nerve-fibres; *secretory fibres* cause the act of secretion, while *trophic fibres* cause chemical processes within the cells, partly resulting in the formation of the soluble constituents of the secretion, and partly in the growth of the protoplasm. According to the number of both kinds of fibres present in a nerve passing to a gland, such nerve being stimulated, the secretion takes place more rapidly (cerebral nerve) or more slowly (sympathetic), while the secretion contains less or more solid constituents. The *cerebral* nerves contain many secretory fibres and few trophic fibres, while the *sympathetic* contain more trophic but few secretory fibres. The rapidity and chemical composition of the secretion vary according to the strength of the stimulus. During continued secretion, the supply of secretory materials in the gland-cells is used up more rapidly than it is replaced by the activity of the protoplasm; hence, the amount of organic constituents diminishes, and the microscopic characters of the cells are altered. The microscopic characters of the cells are altered also by the increase of the protoplasm, which takes place in an active gland. The mucous cells disappear, and seem to be

dissolved after prolonged secretion, and their place is taken by other cells derived from the proliferation of the marginal cells (?). The energy which causes the current of fluid depends upon the protoplasm of the gland-cells."

146. THE SALIVA OF THE INDIVIDUAL GLANDS.—(a) **Parotid saliva** (Steno's duct); it has an *alkaline* reaction, but during fasting, the first few drops may be neutral or even acid on account of free CO_2 ; its specific gravity is 1003 to 1004. [It does not contain any morphological constituents.] After standing it becomes turbid, and deposits, in addition to albuminous matter, calcium carbonate, which is present in the fresh saliva in the form of bicarbonate. It contains small quantities (more abundant in the horse) of a globulin-like body, and never seems to be without CNKS, *i.e.*, sulphocyanide of potassium (or sodium),—which, however, is absent in the sheep and dog.

[The **sulphocyanide** gives a dark red colour (ferric sulphocyanide) with ferric chloride, and the colour is discharged by mercuric chloride, but this is not the case with meconic acid, which gives a similar colour-reaction.] It also reduces iodic acid when added to saliva, causing a yellow colour from the liberation of iodine, which may be detected at once by starch (*Solera*).

Amongst the **organic** substances the most important are **ptyalin**, a small amount of *urea*, and traces of a volatile acid. **Mucin is absent**, hence the parotid saliva is not sticky, and can readily be poured from one vessel into another. It contains 1.5 to 1.6 per cent. of solids in man, of which 0.3 to 1.0 per cent. is inorganic [It does not contain any morphological elements. Its diastatic action is more powerful in man than that of the sub-maxillary gland, or of mixed saliva. Parotid saliva is powerfully diastatic in the rodents (guinea-pig, rat, mouse, rabbit); it is less active in ruminants, and it is said to be inactive in the sheep. It is almost inactive in the dog and cat.]

Of the **inorganic** constituents—the most abundant are potassium and sodium chlorides; then potassium, sodium, and calcium carbonates, some phosphates, and a trace of an alkaline sulphate.

Salivary calculi are formed in the ducts of the salivary glands owing to the deposition of lime-salts, and they contain only traces of the other salivary constituents; in the same way is formed the tartar of the teeth, which contains many threads of leptothrix, and the remains of low organisms which live in decomposing saliva in carious cavities and between the teeth.

Method of obtaining saliva.—In order to obtain the saliva from the individual glands, a thin metallic tube or cannula is introduced into the corresponding duct. On making masticatory movements, or on stimulating the tongue with sapid substances, there is a reflex secretion of saliva which flows out by the tube.

(b) **Sub-maxillary saliva** is obtained by placing a cannula in Wharton's duct; it is alkaline, and may be strongly so. After standing for a time, fine crystals of calcium carbonate are deposited; as also an amorphous albuminous body. It always contains **mucin** (which is precipitated by acetic acid); hence, it is usually somewhat stringy and viscid. It contains **ptyalin**, but in less amount than in parotid saliva; and, according to Oehl, only 0.0036 per cent. of potassium sulphocyanide.

Chemical Composition.—**Sub-maxillary saliva** (dog):

Water,	991.45	per 1000.		
Organic Matter,	2.89			
Inorganic Matter,	5.66		4.50 NaCl and CaCl_2 .	
			1.16 CaCO_3 , Calcium and Magnesium phosphates.	
			Mixed Saliva (Human) (<i>Jacobowitsch</i>).	Parotid (Human) (<i>Hoppe-Seyler</i>).
[Water,			99.51	99.32
Solids,			0.49	0.68
Soluble organic bodies (ptyalin),			0.13	0.34
Epithelium, mucin,			0.16	0.17
Inorganic salts,			0.102	0.34
Potassic sulphocyanide,			0.006	0.03
Potassic and sodic chlorides,			0.084	...
				0.066
				0.43
				...
				...

Gases.—Pflüger found that 100 cubic centimetres of the saliva contained 0.6 O; 64.7 CO₂ (part could be pumped out, and part required the addition of phosphoric acid); 0.8 N; or, in 100 vol. gas, 0.91 O; 97.88 CO₂; 1.21 N. [It therefore contains much more CO₂ than venous blood. Kitz obtained from 100 c.c. of human saliva 7 c.c. of gas—O=1 c.c., N=2.5 c.c. and CO₂=3.5 c.c. Besides this there is 40—60 c.c. of fixed CO₂ in the form of carbonates.]

(c) **Sub-lingual saliva** is obtained by placing a very fine cannula in the ductus Rivinianus; it is *strongly alkaline* in reaction, very sticky and viscid, contains much mucin, numerous salivary corpuscles, and some potassium sulphocyanide.

147. THE MIXED SALIVA IN THE MOUTH.—The mixed saliva in the mouth is a mixture of the secretions from the salivary, mucous and other glands of the mouth.

(1) **Physical Characters.**—It is an opalescent, tasteless, odourless, slightly glairy fluid, with a specific gravity of 1004 to 1009, and an alkaline reaction [due to alkaline bicarbonates and phosphates]. The **amount** secreted in twenty-four hours=200 to 1500 grams (7 to 50 oz.); according to Bidder and Schmidt, however, =1000 to 2000 grams. The solid constituents =5.8 per 1000.

Composition.—The solids are:—Epithelium and mucus, 2.2; ptyalin and albumin, 1.4; salts, 2.2; potassium sulphocyanide, 0.04 per 1000. The ash contains chiefly potash, phosphoric acid, and chlorine (*Hammerbacher*).

Decomposition-products of epithelium, salivary corpuscles, or the remains of food, may render it *acid temporarily*, as after long fasting, and after much speaking; the reaction is acid in some cases of dyspepsia and in fever, owing to the stagnation and insufficient secretion.

(2) **Microscopic Constituents.**—(a) The **salivary corpuscles** are slightly larger than the white blood-corpuscles (8 to 11 μ), and are nucleated protoplasmic globular cells without an envelope (fig. 185). While the corpuscles are living, the particles in their interior exhibit *molecular* or **Brownian movement**. The dark granules lying in the protoplasm are thrown into a trembling movement, from the motion of the fluid in which they are suspended. This dancing motion stops when the cell dies.

[The **Brownian movements** of these suspended granules are purely physical, and are exhibited by all fine microscopic particles suspended in a limpid fluid, *e.g.*, gamboge rubbed up in water, particles of carmine, charcoal, &c.]

(b) **Pavement epithelial cells** from the mucous membrane of the mouth and tongue; they are very abundant in catarrh of the mouth (fig. 185).

(c) **Living organisms**, which live and thrive in the cavities of teeth, nourished by the remains of food. Amongst these are *Leptothrix buccalis* (figs. 171, 185) and small bacteria-like organisms. The threads of the leptothrix penetrate into the canals of the dentine, and produce dental caries. [Miller has found twenty-five varieties of micro-organisms, including cocci (*Iodococcus vaginatus*), bacteria (*Bacillus buccalis maximus*), vibrios, spirilla (*Spirillum sputigenum*), and spirochaete (*Spirochaeta dentium*), eight of them present in the stomach and twelve in the intestines. The Zooglea form of *Leptothrix* forms the yellow scum on the teeth.]

(3) **Chemical Properties.**—(a) **Organic Constituents.**—*Serum-albumin* is precipitated by heat and by the addition of alcohol. In saliva, mixed with much water and shaken up with CO₂, a *globulin-like* body is precipitated; *mucin* occurs in small amount. Amongst the extractives, the most important is **ptyalin**; *fats* and *urea* occur only in traces. In twenty-four hours 130 milligrams of potassium or sodium sulphocyanide are secreted.

[Mucin makes saliva viscid. It is precipitated by acetic acid, but if much NaCl be added an

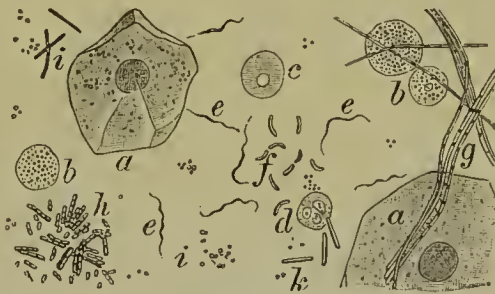


Fig. 185.

Microscopic characters of mixed saliva and the buccal secretion. *a*, epithelial cells; *b*, salivary corpuscles; *c*, fat droplets; *d*, leucocytes; *e*, spirochaeta buccalis; *f*, comma bacillus of the mouth; *g*, *Leptothrix buccalis*; *h*, *i*, *k* different forms of fungi.

excess of acid will not precipitate it. It is a very complex body, but it can be split up into a proteid-like body and a carbohydrate (§ 250, 1).]

(b) **Inorganic Constituents.**—Sodium and potassium chlorides, potassium sulphate, alkaline and earthy phosphates, ferric phosphate.

According to Schönbein, the saliva contains traces of *nitrites* (detected by adding dilute sulphuric acid and diamido-benzol to dilute saliva), which give a yellow colour (*Gries*). There are also traces of ammonia (*Brücke*).

Abnormal Constituents.—In diabetes mellitus, *lactic acid*, derived from a further decomposition of grape-sugar, is found. It dissolves the lime in the teeth, giving rise to diabetic dental caries. *Frerichs* found *leucin*, and *Vulpian* increase of albumin in albuminuria. Of foreign substances taken into the body, the following appear in the saliva:—Mercury, potassium, iodine, and bromine.

Saliva of New-Born Children.—In new-born children, the parotid alone contains ptyalin. The diastatic ferment seems to be developed in the sub-maxillary gland and pancreas, at the earliest, after two months. Hence, it is not advisable to give starchy food to infants. No ptyalin has been found in the saliva of infants suffering from thrush (*Oidium albicans*—*Zweifel*). The diastatic action of saliva is not absolutely necessary for the suckling, feeding as it does upon milk. The mouth during the first two months is not moist, but at a later period saliva is copiously secreted (*Korowin*); after the first six months the salivary glands increase considerably. The eruption of the teeth—owing to the irritation of the mucous membrane—produces a copious secretion of saliva.

148. PHYSIOLOGICAL ACTIONS OF SALIVA.—I. **Diastatic Action.**—The most important chemical action exerted by saliva in digestion is its diastatic or amylolytic action (*Leuchs*, 1831), *i.e.*, the transformation of starch into **dextrin** and some form of **sugar**. This is due to the **ptyalin**—a **hydrolytic ferment or enzyme**—which, even when it is present in very minute quantity, causes starch to take up water and become soluble, the ferment itself undergoing no essential change in the process. [Ptyalin belongs to the group of unorganised ferments (§ 250, 9). Like all other ferments, it acts only within a certain range of temperature, being most active about 40° C. Its energy is permanently destroyed by boiling. It acts best in a slightly alkaline or neutral medium.]

II. Saliva dissolves those substances which are soluble in water; its alkaline reaction enables it to dissolve some substances which are not soluble in water alone, but require the presence of an alkali.

III. Saliva moistens dry food and aids mastication and the formation of the “bolus,” while by its mucin it helps the act of swallowing, the mucin being given off unchanged in the fæces. The ultimate fate of ptyalin is unknown.

[IV. Saliva also aids articulation, and according to *Liebig* it carries down into the stomach small quantities of O.]

[V. It is necessary to the sense of taste to dissolve sapid substances, and bring them into relation with the end-organs of the nerves of taste.]

Saliva has no action on proteids or on fats.

The presence of a peptone-forming ferment has recently been detected in saliva (*Hüfner*, *Munk*, *Kühne*). [Perfectly healthy human saliva has no poisonous properties.]

[**Action of Saliva on Starch.**—**Starch-grains** consist of **granulose** or starch enclosed by coats of **cellulose**. Starch-grains, *e.g.*, of the potato, consist of oval microscopic granules with concentric markings arranged in a lob-sided manner around an eccentrically placed spot, the hilum (fig. 186). Cellulose does not appear to be affected by saliva, so that saliva acts but slowly on raw unboiled starch. If the starch be boiled so as to swell up the starch-grains, and rupture the cellulose envelopes, the amylolytic action takes place rapidly. If starch-paste or starch-mucilage, made by boiling starch in water, be acted upon by saliva, especially at the temperature of the body, the first **physical** change observable is

the liquefaction of the paste, the mixture becoming more fluid and transparent. The change takes place in a few minutes. When the action is continued, important chemical changes occur.]

According to O'Sullivan, Musculus, and v. Mering, the diastatic ferment of saliva (and of the pancreas), by acting upon starch or glycogen, forms **dextrin** and **maltose** (both soluble in water). Several closely allied varieties of dextrin, distinguishable by their colour-reactions, seem to be produced (*Brücke*). **Erythro-dextrin** is formed first, it gives a red colour with iodine; then a reducing dextrin—**achroodextrin**, which gives no colour-reaction with iodine. The sugar formed by the action of ptyalin upon starch is **maltose** ($C_{12}H_{22}O_{11} + H_2O$), which is distinguished from grape-sugar ($C_{12}H_{24}O_{12}$) by containing one molecule less of water, which, however it holds as a molecule of water of hydration. [Maltose also differs from grape-sugar in its greater rotatory power on polarised light, the former = $+150^\circ$, the latter $+56^\circ$, and in its smaller power of reducing euprie oxide, the ratio being 100 : 61. Thus, between the original starch and the final product, maltose, several intermediate bodies are formed. The starch gives a blue with iodine, but after it has been acted on for a time it gives a red or violet colour, indicating the presence of erythro-dextrin, there being a simultaneous production of sugar; but ultimately no colour is obtained on adding iodine—achroodextrin, which gives no colour with iodine,—and maltose being formed. The presence of the maltose is easily determined by testing with Fehling's solution.]

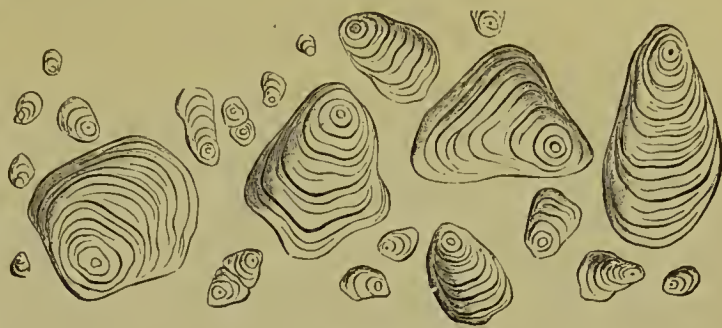
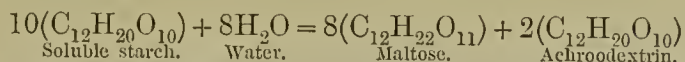


Fig. 186.

Grains of potato-starch $\times 300$.

[Brown and Heron suggest that the final result of the transformation may be represented by the equation—



The ferment slowly changes maltose into grape-sugar or dextrose. This result may be brought about much more rapidly by boiling maltose with dilute sulphuric or hydrochloric acid.] Achroodextrin ultimately passes into maltose, and this again into dextrose; the other form of dextrin does not seem to undergo this change (Seegen's Dystropodextrin). For the further changes that maltose undergoes in the intestine, see § 183, II. 2.

[**Action of Acid on Starch.**—Starch may be converted into dextrin and sugar by boiling it with a dilute acid, *e.g.*, HCl, but there is a difference between this hydration producing an acid and that produced by a ferment like ptyalin. In the former case the sugar produced is wholly dextrose, no maltose being formed.]

[The formula of starch is usually expressed as $C_6H_{10}O_5$, but the researches already mentioned, and those of Brown and Heron, make it probable that it is more complex, which we may provisionally represent by $nC_{12}H_{20}O_{10}$. According to Musculus and Meyer, erythro-dextrin is a mixture of dextrin and soluble starch.]

Preparation of Ptyalin.—(1) Like all other hydrolytic ferments, it is carried down with any copious precipitate that is produced in the fluid which contains it, and it can be isolated from the precipitate. The saliva is acidulated with phosphoric acid, lime-water is added until the reaction becomes alkaline, when a precipitate of the basic calcium phosphate occurs, which carries the ptyalin along with it. This precipitate is collected on a filter, washed with water,

which dissolves the ptyalin, and from its watery solution it is precipitated by alcohol as a white powder. It is redissolved in water and reprecipitated and is obtained pure (*Cohnheim*).

(2) **Glycerin or v. Wittich's Method.**—The salivary glands [rat] are chopped up, placed in absolute alcohol for twenty-four hours, taken out and dried, and afterwards placed in glycerin for several days, which extracts the ptyalin. It is precipitated by alcohol from the glycerin extract.

(3) William Roberts recommends the following solutions for extracting ferments from organs which contain them :—(1) A 3 to 4 per cent. solution of a mixture of 2 parts of boracic acid and 1 part borax. (2) Water, with 12 to 15 per cent. of alcohol. (3) 1 part chloroform to 200 of water.

Conditions affecting the Diastatic Action of Saliva. (*a*) The diastatic or sugar-forming action is known by—(1) **The disappearance of the starch.** When a small quantity of starch is boiled with several hundred times its volume of water, starch mucilage is obtained, which strikes a blue colour with iodine. If to a small quantity of this starch a sufficient amount of saliva be added, and the mixture kept for some time at the temperature of the body, the blue colour disappears. (2) The presence of sugar is proved directly by using the tests for sugar (§ 149).

(*b*) The action takes place more slowly in the *cold* than at the temperature of the body—the action is enfeebled at 55° C., and destroyed at 75° C. (*Paschutin*). The most favourable temperature is 35° to 39° C.

(*c*) The ptyalin itself does not seem to be changed during its action, but ptyalin which has been used for one experiment is less active when used the second time (*Paschutin*).

Ptyalin differs from diastase—the ferment in germinating grains—in so far that the latter first begins to act at + 66° C. Ptyalin decomposes salicin into saligenin and grape-sugar (*Frerichs and Städler*).

(*d*) Saliva acts best in an exactly **neutral medium**, but it also acts in an alkaline and even in a slightly acid fluid; strong acidity prevents its action. The ptyalin is only active in the stomach when the acidity is due to *organic acids* (lactic or butyric), and not when free hydrochloric acid is present (*van de Velde*). In both cases, however, dextrin is formed. Ptyalin is destroyed by hydrochloric acid or digestion by pepsin (*Chittenden and Griswold, Langley*). Even butyric and lactic acids formed from grape sugar in the stomach may prevent its action; but if the acidity be neutralised, the action is resumed (*Cl. Bernard*).

(*e*) The addition of common salt, ammonium chloride, or sodium sulphate (4 per cent. solution), *increases* the activity of the ptyalin, and CO₂, acetate of quinine, strychnia, morphia, enure, 0.025 per cent. sulphuric acid, have the same effect.

(*f*) Much alcohol and caustic potash destroy the ptyalin: long exposure to the air weakens its action, sodium carbonate and magnesium sulphate delay the action (*Pfeiffer*). Salicylic acid and much atropin arrest the formation of sugar.

(*g*) Ptyalin acts very feebly and very gradually upon **raw starch**, only after 2 to 3 hours (*Schiff*); while upon boiled starch it acts rapidly. [Hence the necessity for boiling thoroughly all starchy foods.]

(*h*) The various kinds of starch are changed more or less rapidly according to the amount of cellulose which they contain; raw potato starch after 2 to 3 hours, raw maize starch after 2 to 3 minutes (*Hammarsten*); wheat starch more quickly than that of rice. When the starches are powdered and boiled, they are changed with equal rapidity.

(*i*) A mixture of the saliva from all the glands is more active than the saliva from any single gland (*Jakubowitsch*), while mucin is inactive.

(*j*) The action of ptyalin, like all such ferments, is hindered by the products of its own action. As the sugar accumulates, the action of the ptyalin is slowed or arrested. If the sugar formed be removed the ptyalin again acts on the remainder of the starch.]

[Effect of Tea.]—Tea has an intensely inhibitory effect on salivary digestion, which is due to the large quantity of tannin contained in the tea-leaf. Coffee and cocoa have only a slight effect on salivary digestion. The only way to mitigate the inhibitory effect of tea on salivary digestion is “not to sip the beverage with the meal, but to eat first and drink afterwards” (*Roberts*).]

149. TESTS FOR SUGAR.—1. **Trommer's test** depends upon the fact that, in alkaline solutions, sugar acts as a **reducing agent**; in this case a metallic oxide is changed into a suboxide. To the fluid to be investigated, add $\frac{1}{2}$ of its volume of a solution of caustic potash (soda), specific gravity 1.25, and a few drops of a weak solution of cupric sulphate, which causes at first a bluish precipitate, consisting of hydrated cupric oxide, but it is redissolved, giving a clear blue fluid, if sugar be present. Heat the upper stratum of the fluid, and a yellow or red ring of cuprous oxide is obtained, which indicates the presence of sugar; $2\text{CuO} - \text{O} = \text{Cu}_2\text{O}$.

The solution of hydrated cupric oxide is caused by other organic substances; but the final stage, or the production of cuprous oxide, is obtained only with certain sugars—grape-, fruit-

and milk- (but not cane-) sugar. Fluids which are turbid must be previously filtered, and if they are highly coloured, they must be treated with basic lead acetate; the lead acetate is afterwards removed by the addition of sodium phosphate and subsequent filtration. If very small quantities of sugar are present along with compounds of ammonia, a yellow colour instead of a yellow precipitate may be obtained. In doing the test, care must be taken not to add too much cupric sulphate.

[2. **Fehling's Solution** is an alkaline solution of potassio-tartrate of copper. Boil a small quantity of the deep-blue-coloured Fehling's solution in a test-tube, and add to the boiling test a few drops of the fluid supposed to contain the sugar. If sugar be present, the copper solution is reduced, giving a yellow or reddish precipitate. The reason for boiling the test itself is, that the solution is apt to decompose when kept for some time, when it is precipitated by heat alone. This is one of the best and most reliable tests for the presence of sugar. In Pavy's modification of this test, ammonia is used instead of a caustic alkali (§ 267).]

(3) **Böttger's Test.**—Alkaline bismuth oxide solution is best prepared, according to Nylander, as follows:—2 grms. bismuth subnitrate, 4 grms. potassic and sodic tartrate, 100 grms. caustic soda of 8 per cent. Add 1 c.c. to every 10 c.c. of the fluid to be investigated. When boiled for several minutes, the sugar causes the reduction and deposits a black precipitate of metallic bismuth. [According to Salkowski the urine of a person taking rhubarb gives the same reaction with this test.]

(4) **Moore and Heller's Test.**—Caustic potash or soda is added until the mixture is strongly alkaline; it is afterwards boiled. If sugar be present, a yellow, brown, or brownish-black coloration is obtained. If nitric acid be added, the odour of burned sugar (caramel) and formic acid is obtained.

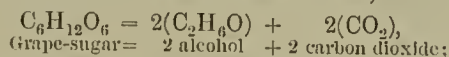
(5) **Mulder and Neubauer's Test.**—A solution of indigo-carmin, rendered alkaline with sodic carbonate, is added to the sugar solution until a slight bluish colour is obtained. When the mixture is heated, the colour passes into purple, red, and yellow. When shaken with atmospheric air, the fluid again becomes blue.

Molisch's Test.—To 5 c.cm. of the fluid add 2 drops of a 17 per cent. alcoholic solution of α -naphthol, or a solution of thymol. Add 1 to 2 c.cm. of concentrated sulphuric acid, and shake the mixture. The presence of sugar colours the α -naphthol mixture deep violet, the thymol deep red. The subsequent addition of water causes a precipitate of similar colour, which is insoluble in concentrated hydrochloric acid. Albumin, casein, and peptone give the same reaction (*See* *gen*), but the deposit on the addition of water is soluble in concentrated hydrochloric acid.

Other tests, including the **Phenyl-hydrazin test**, are described in § 267.

In all cases where albumin is present it must be removed—in urine by acidulating with acetic acid and boiling; in blood, by adding four times its volume of alcohol and afterwards filtering, while the alcohol is expelled by heat. [If peptone be present the cuprous oxide may not be precipitated on boiling. The mixture must be evaporated down, the sugar dissolved out by alcohol, and the test for sugar applied to a watery solution of the alcoholic extract.]

150. QUANTITATIVE ESTIMATION OF SUGAR.—I. By Fermentation.—In the glass vessel (fig. 187, *a*) a measured quantity (20 c.cm.) of the fluid (sugar) is placed along with some yeast, while *b* contains concentrated sulphuric acid. The whole apparatus is then weighed. When exposed to a sufficient temperature (10° to 40° C.), the sugar splits into 2 molecules of alcohol and 2 of carbon dioxide,



and in addition there are formed traces of glycerin and succinic acid. The CO_2 escapes from *b*, and as it passes through the H_2SO_4 , the CO_2 yields to the latter its water. The apparatus is weighed after two days, when the reaction is ended, and the amount of sugar is calculated from the loss of weight in the 20 c.cm. of fluid. 100 parts of water-free sugar = 48.89 parts CO_2 , or 100 parts CO_2 correspond to 204.54 parts of sugar.

II. Titration.—By means of Fehling's solution, which is made of such a strength that all the copper in 10 cubic centimetres of the solution is reduced by 0.05 grams of grape-sugar (§ 267).

III. Circumpolarisation.—The saccharimeter of Soleil-Ventzke may be used to determine the amount of sugar present. It may also be used for the quantitative estimation of albumin. Sugar rotates the ray of polarised light to the right and albumin to the left. The amount of

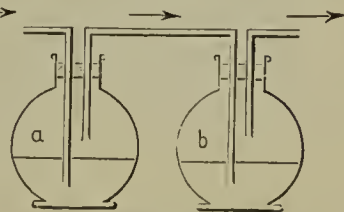


Fig. 187.

Apparatus for the quantitative estimation of sugar by fermentation.

rotation, or "specific rotatory power," is directly proportional to the amount of the rotating substance present in the solution, so that the amount of rotation of the ray indicates the amount of the substance present. By the term "specific rotatory power" is meant the degree of rotation which is produced by 1 gram. of the substance dissolved in 1 c.cm. of water, when examined in a layer 1 decimetre thick. For yellow light the specific rotation of grape-sugar is $+56^\circ$.

In fig. 188 the light from the lamp falls upon a crystal of calc-spar. Two Nicol's prisms are placed at *v* and *s*, *v* is movable round the axis of vision, while *s* is fixed. In *m* Soleil's double

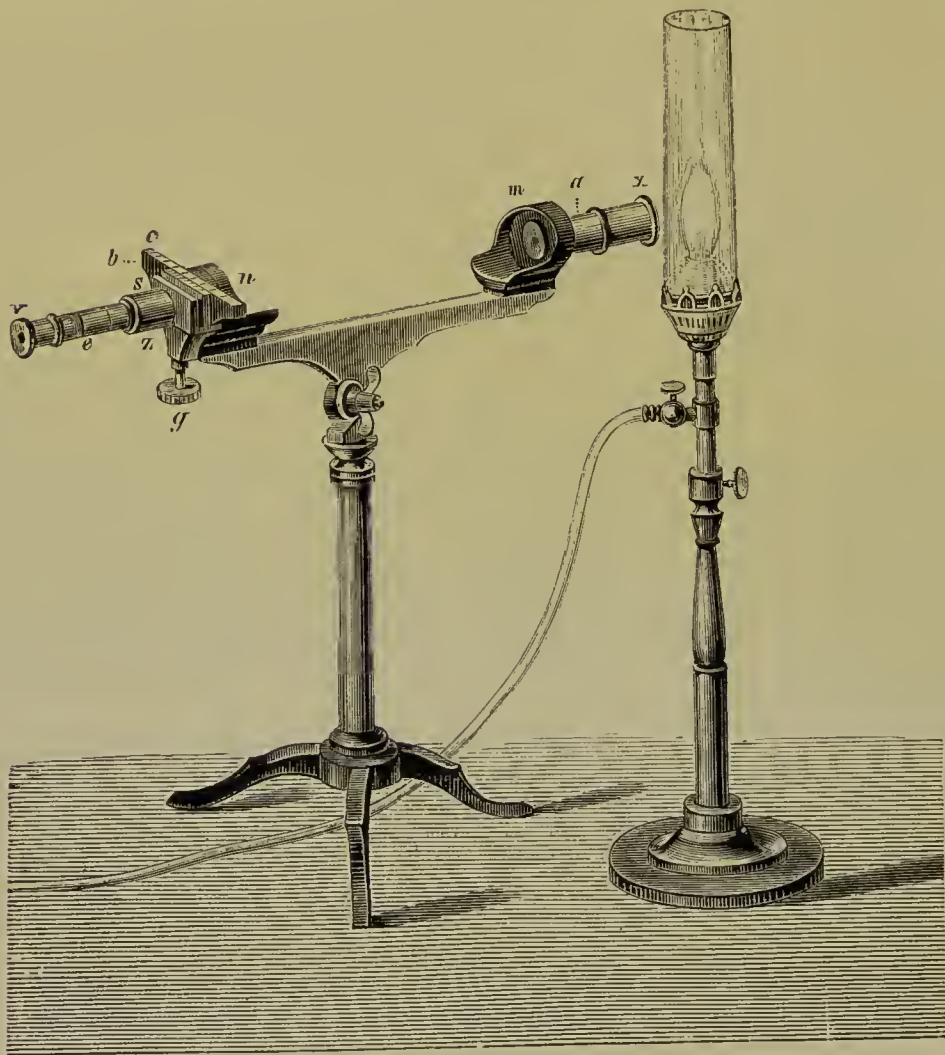


Fig. 188.

Soleil-Ventzke's polarisation apparatus.

plate of quartz is placed, so that one-half of it rotates the ray of polarised light as much to the right as the other rotates it to the left. In *n* the field of vision is covered by a plate of *left-rotatory* quartz. At *b c* is the *compensator*, composed of two right-rotatory prisms of quartz, which can be displaced laterally by the milled head, *g*, so that the polarised light passing through the apparatus can be made to pass through a thicker or thinner layer of quartz. When these right-rotatory prisms are placed in a certain position, the rotation of the left-rotatory quartz at *n* is exactly neutralised. In this position the scale on the compensator has its numerus exactly at *o*, and both halves of the double plate at *m* appear to have the same colour to the observer, who from *v* looks through the telescope placed at *e*. Rotate the Nicol's prism at *v* until a bright rose-coloured field is obtained. In this position the telescope must be so adjusted that the vertical line bounding the two halves shall be distinctly visible. The apparatus is now ready for use.

Fill a tube, 1 decimetre in length, with urine containing sugar or albumin, the urine being perfectly clear. The tube is placed between *m* and *n*. By rotating the Nicol's prisms, *v*, the rose-colour is again obtained. The compensator at *g* is then rotated until both halves of the field of vision have exactly the same colour. When this is obtained, read off on the scale the number of degrees the nonius is displaced to the right (sugar) or to the left (albumin) from zero. The number of degrees indicates directly the number of grams of the rotating substance present in 100 c.c. of the fluid. If the fluid is very dark coloured, it must be decolorised by filtering it through animal charcoal (*Seegen*), [or the colouring matter may be precipitated by the addition of lead acetate.] If the sugary urine contains albumin, the latter must be removed by boiling and filtration. A turbidity not removed by filtration may be got rid of by adding a drop of acetic acid or several drops of sodic carbonate or milk of lime, and afterwards filtering. [One may also employ the apparatus of Mitscherlich, or the "half-shadow apparatus" of Laurent.]

151. MECHANISM OF THE DIGESTIVE APPARATUS.—This embraces the following acts:—

1. The introduction and mastication of the food; the movements of the tongue; insalivation; formation of the bolus of food.
2. Deglutition.
3. The movements of the stomach, small and large intestine.
4. The excretion of faecal matters.

152. INTRODUCTION OF THE FOOD.—Fluids are taken into the mouth in three ways:—(1) By **suction**, the lips are applied air-tight to the vessel containing the fluid, while the tongue is retracted (the lower jaw being often depressed) and acts like the piston in a suction-pump, thus causing the fluid to enter the mouth. Herz found that the negative pressure caused by an infant while sucking = 3 to 10 mm. Hg. (2) The fluid is **lapped** when it is brought into direct contact with the lips, and is raised by aspiration and mixed with air so as to produce a characteristic sound in the mouth. (3) Fluid may be **poured** into the mouth, and as a general rule, the lips are applied closely to the vessel containing the fluid.

Solids, when they consist of small particles, are licked up with the lips, aided by the movements of the tongue. In the case of large masses, a part is bitten off with the incisor teeth, and is afterwards brought under the action of the molar teeth by means of the lips, cheeks, and tongue.

153. MASTICATION.—The process of mastication is a complicated co-ordinate muscular act carried out under the direction of the central nervous system, with the aid of guiding sensations originating in the structures of the mouth.

The articulation of the jaw is provided with an interarticular cartilage—the meniscus—which prevents direct pressure being made upon the articular surface when the jaws are energetically closed, and which also divides the joint into two cavities, one lying over the other. The capsule is so lax that, in addition to the raising and depressing of the lower jaw, it permits of the lower jaw being displaced forwards, whereby the meniscus moves with it, and covers the articular surface.

The **process of mastication** embraces:—(a) The **elevation of the jaw**, accomplished by the combined action of the Temporal, Masseter, and Internal Pterygoid Muscles. If the lower jaw was previously so far depressed that its articular surface rested upon the tubercle, it now passes backwards upon the articular surface.

(b) The **depression of the lower jaw** is caused by its own weight, aided by the action of the anterior bellies of the Digastrics, the Mylo- and Genio-hyoid and Platysma. The muscles act especially during forcible opening of the mouth. The necessary fixation of the hyoid bone is obtained through the action of the Omo- and Sterno-hyoid, and by the Sterno-thyroid and Thyro-hyoid.

When the articular surface of the lower jaw passes forwards on to the tubercle, the External Pterygoids actively aid in producing this (*Bérard*).

(c) **Displacement of the Articular Surfaces.**—During rest, when the mouth is closed, the incisor teeth of the lower jaw are within the arch of the upper incisors. When in this position the jaw is protruded by the External Pterygoids, whereby the

articular surface passes onto the tubercle (and, therefore, downwards), while the lateral teeth are thereby separated from each other. The jaw is retracted by the Internal Pterygoids without any aid from the posterior fibres of the Temporals. When one articular surface is carried forwards, the jaw is protruded and retracted by the External and Internal Pterygoid of the same side. At the same time, there is a transverse movement, whereby the back teeth of the protruded side are separated from each other.

During mastication, the individual movements of the lower jaw are variously combined, and especially with lateral grinding movements, while the food to be masticated is kept from passing outwards by the action of the muscles of the lips (*Orbicularis oris*) and the *Buccinators*, while the tongue continually pushes the particles between the molar teeth. The energy of the muscles of mastication is regulated by the **sensibility of the teeth**, and the muscular sensibility of the muscles of mastication, as well as by the general sensibility of the mucous membrane of the mouth and lips. At the same time, the mass is mixed with saliva, the divided particles cohere, and are formed into a mass or **bolus**, of a long, oval shape, by the muscles of the tongue. The bolus then rests on the back of the tongue, ready to be swallowed.

Nerves of Mastication.—The muscles of mastication receive their **motor** nerves from the third branch of the trigeminus, the mylo-hyoid and the anterior belly of the digastric being supplied from the same source. The genio-, omo-, and sterno-hyoid, sterno-thyroid, and thyro-hyoid are supplied by the hypoglossal, while the facial supplies the posterior belly of the digastric, the stylo-hyoid, the platysma, the buccinator, and the muscles of the lips. The general centre for the muscles of mastication lies in the medulla oblongata (§ 367).

When the mouth is closed, the jaws are kept in contact by the pressure of the air, as the cavity of the mouth is rendered free from air, and the entrance of air is prevented anteriorly by the lips and posteriorly by the soft palate. The pressure exerted by the air is from 2 to 4 mm. Hg. (*Metzger and Donders*).

[**Effect on the Circulation.**—Marey found that mastication trebled the velocity of the blood-current in the carotid (horse), while François-Frank observed that the circulation of the brain (in man) is increased; hence it is evident that mastication implies an increased supply of blood to the nerve-centres.]

154. STRUCTURE AND DEVELOPMENT OF THE TEETH.—[Each tooth consists of a portion above the gum and termed the **crown**, a part imbedded in the gum, the **fang**, and a narrow **neck** connecting these two.] A **tooth** is just a papilla of the mucous membrane of the gum, which has undergone a characteristic development. In its simplest form, as in the teeth of the lamprey, the connective-tissue basis of the papilla is covered with many layers of corneous epithelium. In **human teeth**, part of the papilla is transformed into a layer of calcified **dentine**, while the epithelium of the papilla produces the **enamel**, the fang of the tooth being covered by a thin accessory layer of bone, the **crusta petrosa** or **cement**.

The **dentine** or ivory which surrounds the pulp-cavity and the canal of the fang (fig. 189) is very firm, elastic, and brittle. Dentine, like the matrix of bone, when treated in a certain way, presents a fibrillar structure. It is permeated by innumerable long, tortuous, wavy tubes—the **dentinal tubules**—each of which communicates with the pulp-cavity by means of a fine opening, and passes more or less horizontally outwards as far as the outer layers of the dentine. The tubules are bounded by an extremely resistant, thin, cuticular membrane, which strongly resists the action of chemical reagents. These tubules are filled completely by soft fibres, the "**fibres of Tomes**," which are merely greatly elongated and branched processes of the **odontoblasts** of the pulp.

The dentinal tubules, as well as the fibres of Tomes, anastomose throughout their entire extent by means of fine processes. As the fibres approach the enamel, which they do not penetrate, some of them bend on themselves, and form a loop (fig. 192, *c*), whilst others pass into the "**interglobular spaces**" (fig. 191), which are so abundant in the outer part of the dentine. The interglobular spaces are

small spaces bounded by curved surfaces. Certain curved lines, "**Schreger's lines**," may be detected with the naked eye in the dentine (*e.g.*, of the elephant's tusk) running parallel

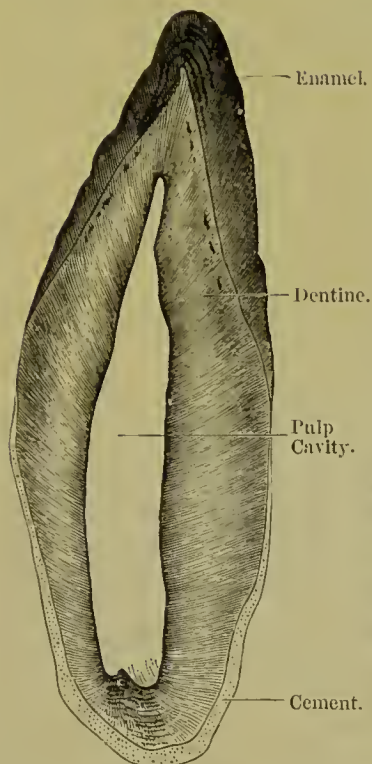


Fig. 189.

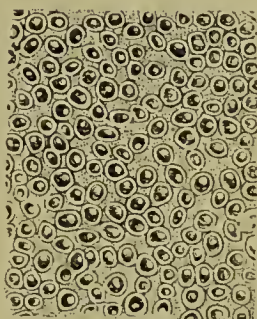


Fig. 190.



Fig. 191.

Fig. 189.—Longitudinal section of an incisor tooth. Fig. 190.—Transverse section of dentine. The light rings are the walls of the dentinal tubules; the dark centres with the light points are the fibres of Tome lying in the tubules. Fig. 191.—Interglobular spaces in dentine.

with the contour of the tooth. They are caused by the fact that at these parts all the chief curves in the dentinal tubules follow a similar course.

The **enamel**, the hardest substance in the body (resembling apatite), covers the crown of the teeth. It consists of

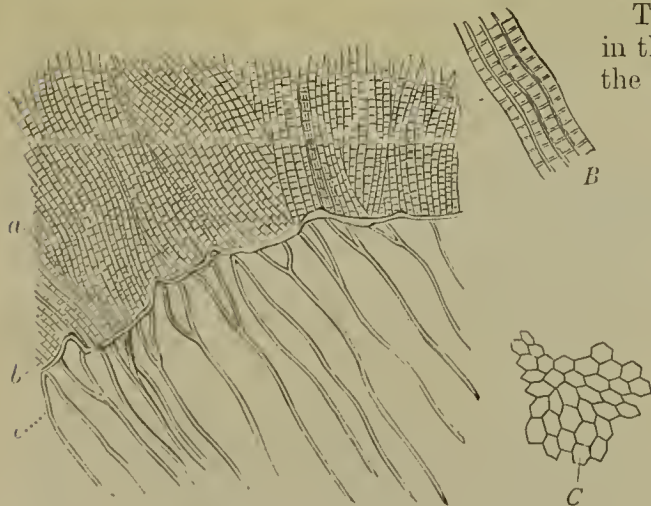


Fig. 192.

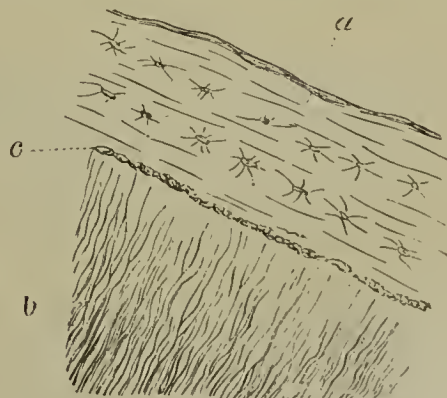


Fig. 193.

Fig. 192.—Section of a tooth between the dentine and enamel. *a*, enamel; *b*, dentinal tubules; *B*, enamel prisms highly magnified; *C*, transverse sections of enamel prisms. Fig. 193.—Transverse section of the fang. *a*, cement with bone-corpuscles; *b*, dentine with tubules; *c*, boundary between both.

hexagonal flattened prisms arranged side by side like a palisade (fig. 192, *B* and

C). They are 3 to 5 μ ($\frac{1}{50000}$ inch) broad, not quite uniform in thickness, curved slightly in different directions, and, owing to inequalities of thickness, they exhibit transverse markings. They are elongated **calcified, cylindrical, epithelial cells**. Retzius described dark-brown lines running parallel with the outer boundary of the enamel, due to the presence of pigment (fig. 189). The fully-formed enamel is negatively doubly refractive and uniaxial, while the developing enamel is positively doubly refractive (*Hoppe-Seyler*).

The **cuticula** or **Nasmyth's membrane** covers the free surface of the enamel as a completely structureless membrane 1 to 2 μ thick, but in quite young teeth it exhibits an epithelial structure, and is derived from the outer epithelial layer of the enamel organ.

The **cement** or **crusta petrosa** is a thin layer of bone covering the fang (fig. 193, a). The bone lacunæ communicate directly with the dental tubules of the fang. Haversian canals and lamellæ are only found where the layer of cement is thick, and the former may communicate with the pulp-cavity. Very thin layers of cement may be devoid of bone-corpuscles. Sharpey's fibres occur in the cement of the dog's tooth; while in the horse's tooth single bone-corpuscles are surrounded by a capsule. In the **periodontal membrane**, which is just the periosteum of the alveolus, coils of blood-vessels similar to the renal glomeruli occur. They anastomose with each other, and are surrounded by a delicate capsule of connective-tissue.

The **pulp** in a fully-grown tooth represents the remainder of the dental papilla around which the dentine was deposited. It consists of a very vascular indis-

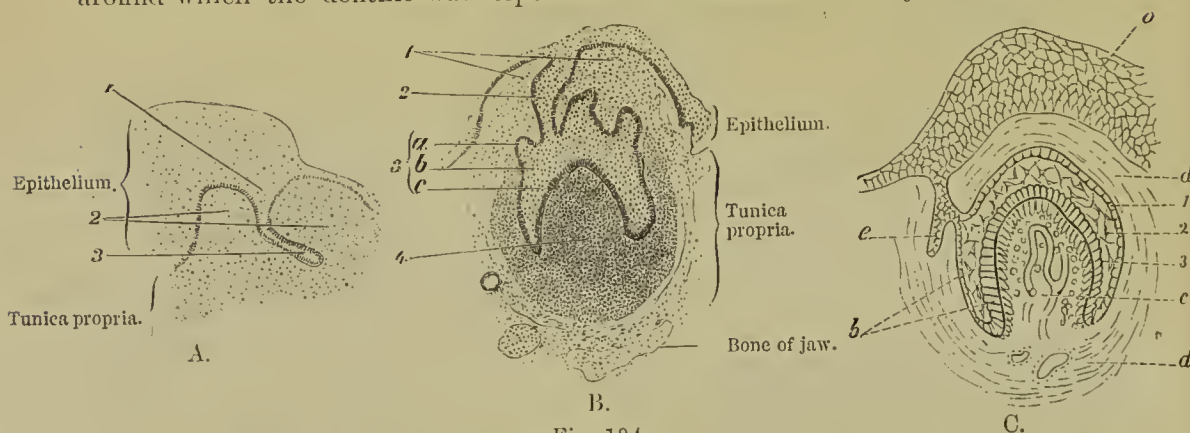


Fig. 194.

A.—Vertical section of the jaw of a sheep embryo $\times 40$. 1, dental furrow; 2, dental ridge; 3, enamel germ. B.—Transverse section of the lower jaw of a four months' human fetus $\times 40$. 1, dental ridge; 2, stalk of the enamel organ; 3, enamel organ; a, peripheral cells, b, germ pulp; c, cylindrical cells of enamel; 4, papilla. C.—a, dental ridge; b, enamel organ with (1) outer epithelium, (2) middle stellate layer, (3) enamel prism-cell layer; c, dentine germ with blood-vessels, and the long osteoblasts on the surface; d, tooth-sac; e, secondary enamel germ.

tinctly fibrillar connective tissue, laden with cells. The layers of cells, resembling epithelium, which lie in direct contact with the dentine, are called **odontoblasts**, *i.e.*, those cells which build up the dentine. These cells send off long branched processes into the dentinal tubules, whilst their nucleated bodies lie on the surface of the pulp, and form connections by processes with other cells of the pulp and with neighbouring odontoblasts. Numerous non-medullated nerve-fibres (sensory from the trigeminus), whose mode of termination is unknown, occur in the pulp.

The **periosteum** or **periodontal membrane** of the fang is, at the same time, the alveolar periosteum, and consists of connective tissue with elastic fibres and many nerves.

Chemistry of a Tooth.—The teeth consist of a gelatine-yielding matrix infiltrated with calcium phosphate and carbonate (like bone). (1) The **dentine** contains—organic matter, 27·70; calcium phosphate and carbonate, 72·06; magnesium phosphate, 0·75; with traces of iron, fluorine, and sulphuric acid.

(2) The **enamel** contains an organic proteid matrix allied to the substance of epithelium. It consists of 3·60 organic matter and 96·00 of calcium phosphate and carbonate, 1·05 magnesium phosphate, with traces of calcium fluoride and an insoluble chlorine compound.

(3) The **cement** is identical with bone.

The **gums** are devoid of mucous glands, very vascular, and often provided with long vascular papillae, which are sometimes compound.

Development of a Tooth.—It begins at the end of the second month of foetal life. Along the whole length of the foetal gum is a thick projecting ridge composed of many layers of epithelium (fig. 194 A). A depression, the **dental groove**, also filled with epithelium, occurs in the gum, and runs along under the ridge. The dental groove becomes deeper throughout its entire length, and on transverse section presents the appearance of a dilated flask, while at the same time it is filled with elongated epithelial cells, which form the "**enamel organ**," or "**common enamel germ**." A conical papilla, the "**dentine germ**," grows up from the mucous tissue, of which the gum consists, towards the enamel organ (figs. 194 B, 194 C), so that the apex of the papilla comes to have the enamel organ resting upon it like a double cap. Afterwards, owing to the development of connective tissue, the parts of the enamel organ lying between and uniting the individual dentine germs, disappear, and gradually the connective-tissue forms a **tooth sac** enclosing the papilla and its enamel organ (fig. 194 A, 3).

Those epithelial cells (figs. 194, B, 3, 194 C) of the enamel organ, which lie next the top of the papilla, are cylindrical, and become calcified to form enamel prisms. The layer of cells of the double cap, which is directed towards the tooth-sac, becomes flattened, fuses, undergoes a

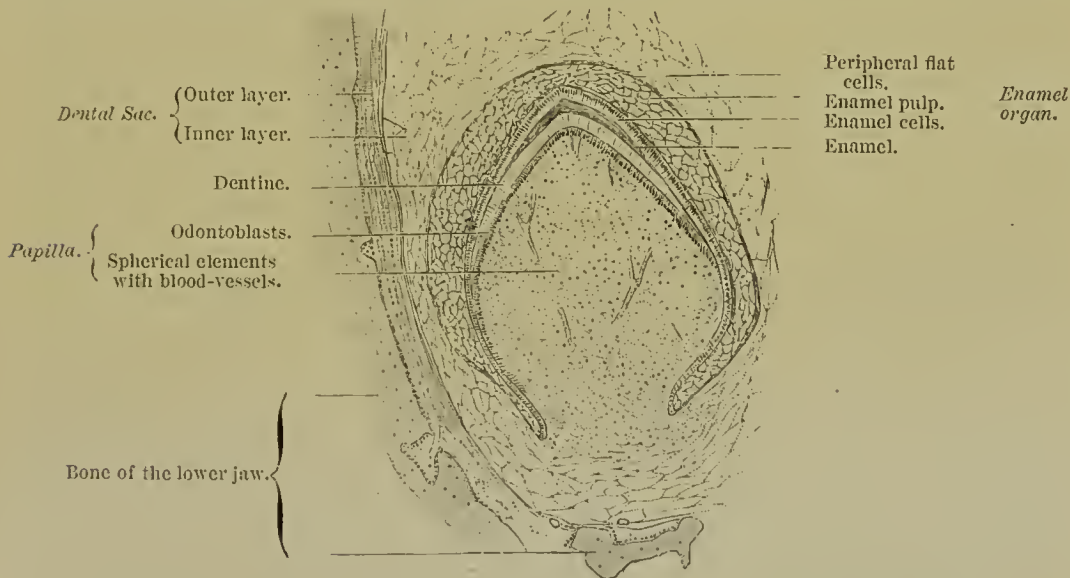


Fig. 195.

Transverse section of the lower jaw of a new-born dog $\times 40$. The dental sac is shown only on the left side. The tissues originating from connective tissue are shown on the left, and those of epithelial origin on the right.

horny transformation, and becomes the **cuticula**, whilst the cells which lie between both layers undergo an intermediate metamorphosis, so that they come to resemble the branched stellate cells of the mucous tissue, and gradually disappear altogether.

The **dentine** is formed in the most superficial layer of the projecting connective tissue of the dental papilla, owing to the calcification of the continuous layer of odontoblasts which occur there (figs. 194 C, 195). During the process, fibres or branches of these cells are left unaffected, and remain as the fibres of Tomes. Exactly the same process occurs as in the formation of bone, the odontoblasts forming around themselves a calcified matrix. The **cement** is formed from the soft connective-tissue of the dental alveolus.

Dentition.—During the development of the first, **temporary** or **milk-teeth** a special enamel organ (fig. 194, c) is formed near these, but it does not undergo

development until the milk-teeth are shed; even the papilla is wanting at first. When the **permanent** tooth begins to develop, it opens into the alveolar wall of the milk-teeth from below. The tissue of this dental sac causes erosion, or eating away of the fang and even of the body of the milk-teeth, without its blood-vessels undergoing atrophy. The chief agents in the absorption are the amœboid cells of the granulation tissue. [Multinuclear giant-cells also erode the fangs of the teeth. The little cavities in which the large osteoclasts lie are known as **Howship's lacunæ** or **foveæ**.]

Eruption of the Milk-Teeth.—The following is the order in which the twenty milk-teeth cut the gum, *i.e.*, from the seventh month to the second year:—Lower central incisors, upper central incisors, upper lateral incisors, lower lateral incisors, first molar, canine, the second molars.

[The figures indicate in **months** the period of eruption of each tooth.]

Molars.	Canines.	Incisors.	Canines.	Molars.
24 12	18	9 7 7 9	18	12 24

[The **permanent teeth** succeed the milk-teeth, the process beginning about the *seventh year*. Ten teeth in each jaw take the place of the milk-teeth, while six teeth appear further back in each jaw. Thus the total number of permanent teeth is thirty-two. As the sacs, from which the permanent teeth are developed, are formed before birth, they merely undergo the same process of development as the temporary teeth, only at a much later period. The last of the permanent molars—the *wisdom-tooth*—may not cut the jaw until the *seventeenth to the twenty-fifth year*. At the sixth year the jaw contains the largest number of teeth, as all the temporary teeth are present, and, in addition, the crowns of all the permanent teeth, except the wisdom-teeth, making forty-eight in all (fig. 196).]

[Eruption of Permanent Teeth.—The age at which each tooth cuts the gum is given in **years** in the following table:—

Molars.	Bicuspid.	Canines.	Incisors.	Canines.	Bicuspid.	Molars.
17 12 to to 6 25 13	10 9	11 to 12	8 7 7 8	11 to 12	9 10	12 17 6 to to 13 25

[Action of Drugs on the Teeth.—All the conditions for putrefaction are present in the mouth; and when putrefaction occurs, the products (often acid) attack the dentine and hasten its decay. Hence, the necessity for thorough daily cleansing of the teeth and mouth. The teeth may be cleaned by means of a soft tooth-brush and water, with or without the use of any of the numerous dentrifices, such as powdered chalk or charcoal. Astringents such as catechu and arca-nut are sometimes used. Mineral acids attack the teeth, and ought when taken to be sucked through a tube.]

155. MOVEMENTS OF THE TONGUE.—The **tongue**, being a muscular organ, and extremely mobile, plays an important part in the process of mastication:—(1) It keeps the food from passing from between the molar teeth. (2) It forms into a bolus the finely-divided food after it is mixed with saliva. (3) When the tongue is raised, the bolus lying on its dorsum is pushed backwards into the pharynx and œsophagus.

The **course of the fibres** is threefold—*longitudinally*, from base to tip; *transversely*, the fibres for the most part proceeding outwards from the vertically-placed septum lingue; *vertically*, from below upwards. Some of the muscles are

confined to the tongue (**intrinsic**), while others (**extrinsic**) are attached beyond it to the hyoid bone, lower jaw, the styloid process, and the palate.

[**The extrinsic Muscles of the tongue.**—The tongue is divided vertically by a fibrous *septum*, and on each side there are four extrinsic muscles. The *hyo-glossus* passes from the hyoid bone upwards into the tongue between the lingualis and stylo-glossus. When both muscles contract the tongue is drawn backwards. The *genio-hyo-glossus* arises from the inner aspect of the anterior part of the ramus of the lower jaw, its fibres spread out in a fan-shaped manner, some going to the hyoid bone, a few to the pharynx, but most enter the entire length of the tongue near the fibrous septum. Both muscles acting together protrude the tongue. The *palato-glossus*, in the anterior pillar of the fauces, enters the upper surface of the tongue, and is concerned in deglutition. The *stylo-glossus* passes from the styloid process down to the side of the tongue. These muscles pull back the tongue and raise its margins.]

[**The intrinsic muscles.**—The *superior* or *superficial lingual* runs from the tip of the tongue towards the hyoid bone just under the mucous membrane. The *transverse muscle*, whose fibres run transversely from the septum to the sides of the tongue. The *vertical* fibres run in an arched direction downwards and outwards towards the dorsum of the tongue. The *inferior* or *deep lingual muscle* consists of a thick bundle of longitudinal fibres running along the under surface between the *genio-hyo-glossus* and the *hyo-glossus*. They shorten the tongue and turn its tip downwards.]

Microscopically, the fibres are transversely striated, with a delicate sarcolemma, and very often they are branched where they are inserted into the mucous membrane. The muscular bundles cross each other in various directions, and in the interspaces fat-cells and glands occur.

Changes in form and position of the tongue :—

(1) *Shortening and broadening* by the longitudinal muscle, aided by the *hyo-glossus*.

(2) *Elongation and narrowing*, by the *transversus linguae*.

(3) *The dorsum is rendered concave* by the *transversus* and the simultaneous action of the median vertical fibres.

(4) *Arching of the dorsum* :—(a) Transversely, by the lowest transverse bundles ; (b) longitudinally, by the lowest longitudinal muscles.

(5) *Protrusion*, by the *genio-glossus*, while at the same time the tongue usually becomes narrower and longer (2).

(6) *Retraction*, by the *hyo-glossus* and *stylo-glossus*, and (1) usually occurring at the same time.

(7) *Depression* into the floor of the mouth, by the *hyo-glossus*. The floor of the mouth may be made deeper by depressing the hyoid bone.

(8) *Elevation* of the tongue towards the palate :—(a) At the tip by the anterior part of the longitudinal fibres ; (b) in the middle by elevating the entire hyoid bone by the *mylo-hyoid* (*N. trigeminus*) ; (c) at the root by the *stylo-glossus* and *palato-glossus*, as well as indirectly by the *stylo-hyoid* (*N. facialis*).

(9) *Lateral movements*, the tip of the tongue passing to the right or left ; these are caused by the longitudinal fibres of one side.

The motor nerve of the tongue is the *hypoglossal* (fig. 197). When this nerve is divided or paralysed on one side, the tip of the tongue lying in the floor of the mouth is directed towards the sound side, because the tonus of the non-paralysed longitudinal fibres shortens the sound

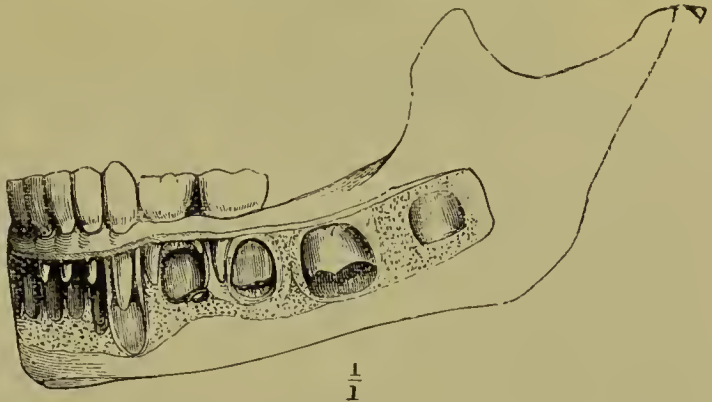


Fig. 196.

Lower jaw of a child, five years of age, with the surface removed to show the unerupt permanent tooth-germs.

side slightly. If the tongue be *protruded*, however, the tip passes towards the *paralysed* side. This arises from the direction of the *genio-glossus* (from the middle downwards and outwards), and the tongue follows the direction of its action. The tongues of animals which have been killed exhibit fibrillar contractions of the muscles, sometimes lasting for a whole day. [Stirling has frequently found nerve-ganglia in the nerves of the tongue.]

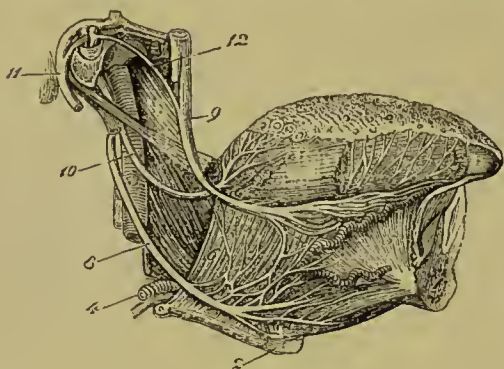


Fig. 197.

The three nerves of the tongue, showing their curved course and their terminations. 1, Mandible; 2, hyoid bone; 3, internal carotid; 4, lingual artery; 5, genio-glossus; 6, hyo-glossus; 7, stylo-glossus; 8, hypoglossal nerve; 9, lingual branch of fifth nerve; 10, glosso-pharyngeal; 11, facial nerve; 12, chorda tympani.

with the nose, mouth and larynx (fig. 198). It is lined by a mucous membrane, and strengthened and made contractile externally by a layer of striped muscular fibres running, for the most part,

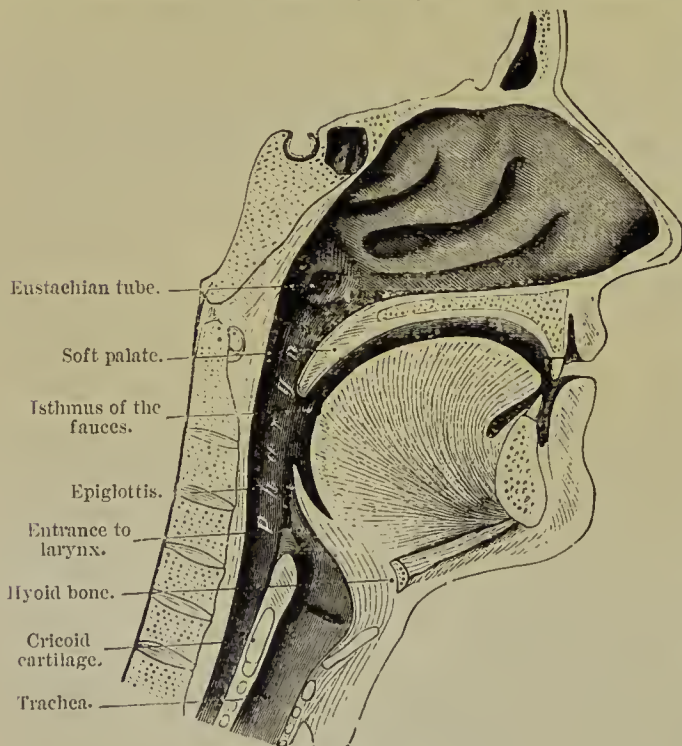


Fig. 198.

Vertical or sagittal median section through the mouth and pharynx.

the fauces, the former containing the *palato-glossus muscle*, and the latter the *palato-pharyngeus muscle*. On each side between the pillars lies a tensil.]

[The *sensory nerves* are the *lingual* or *gustatory branch of the fifth*, which confers sensibility on the mucous membrane of the anterior two-thirds of the tongue. The *lingual branch of the glosso-pharyngeal*, which confers ordinary sensibility and the sense of taste on the posterior third of the tongue. The *chorda tympani*, which is the special nerve of taste for the anterior two-thirds of the tongue. There are also *sympathetic fibres* on the blood-vessels (fig. 197).]

156. DEGLUTITION.—[By a complicated series of co-ordinated muscular acts the bolus of food is carried from the mouth successively through the pharynx and œsophagus into the stomach.]

[The *pharynx* (112 mm. in length) extends from the base of the skull to the lower border of the cricoid cartilage, where it becomes continuous with the œsophagus. Above, it communicates somewhat transversely, and made up of the three *constrictor muscles*, — *superior*, *middle* and *inferior*. Running more longitudinally and internally are the *palato-pharyngeus* and *stylopharyngeus muscles*. Outside the muscular layer of the pharynx is a fibrous or connective-tissue layer. The upper part of the mucous membrane of the pharynx is lined by columnar ciliated epithelium, while that portion opposite and below the fauces is lined by stratified squamous epithelium. Much adenoid tissue also exists in the mucous membrane.]

[Seven openings communicate with the pharynx, viz., the two posterior nares, the isthmus of the fauces, the opening into the larynx, the œsophagus, and the two Eustachian tubes, so that during deglutition all these apertures have to be guarded in some way or other.]

[Anatomically the other important parts are the soft palate with the uvula, the isthmus of the fauces opening from the mouth into the pharynx, and bounded laterally by the anterior and posterior pillars of

The onward movements of the contents of the digestive canal are effected by a special kind of action whereby the tube or canal contracts upon its contents, and as this contraction proceeds along the tube, the contents are thereby carried along. This is the "**peristaltic movement**," or peristalsis.

[The act of swallowing a solid mass has been variously described,—firstly, as consisting of a **voluntary** and an **involuntary stage**. In the **voluntary stage** the food remains in the mouth, but when it reaches the posterior third of the tongue, or rather at the isthmus of the fauces, the **involuntary stage** commences, which includes its passage through the pharynx and œsophagus into the stomach. Others, again, divide it into **three stages**—

- (1) While the food traverses the isthmus of the fauces.
- (2) While the food traverses the pharynx. This includes the movements of the pharynx, the shutting off of the posterior nares, the occlusion of the entrance to the glottis, and the shutting of the pillars of the fauces.
- (3) While it traverses the œsophagus. In this stage gravity has no effect, as the food is carried downwards by peristaltic action of the œsophagus, so that a person can swallow when standing on his head.]

In the act of deglutition, we distinguish in order the following individual movements :—

I. **Voluntary Stage.**—(1) The aperture of the mouth is closed by the orbicularis oris (*N. facialis*).

(2) The jaws are pressed against each other by the muscles of mastication (*N. trigeminus*), while at the same time the lower jaw affords a fixed point for the action of the muscles attached to it and the hyoid bone.

(3) The tip, middle, and root of the tongue, one after the other, are pressed against the hard palate, whereby the contents of the mouth are propelled towards the pharynx [the floor of the mouth being raised by the contraction of the mylohyoid muscles].

II. **Involuntary Stage.**—(4) *The food is prevented from passing into the mouth.* When the bolus has passed the anterior palatine arch (the mucus of the tonsillar glands making it slippery again), it is prevented from returning to the mouth by the palato-glossi muscles which lie in the anterior pillars of the fauces, coming together like two side-screens or curtains, meeting the raised dorsum of the tongue (stylo-glossus).

(5) *The food is prevented from passing into the posterior nares.* The morsel is now behind the anterior palatine arch and the root of the tongue, and has reached the pharynx, where it is subjected to the successive action of the three pharyngeal constrictor muscles which propel it onwards. The action of the superior constrictor of the pharynx is always combined with a horizontal elevation (*Levator veli palatini*; *N. facialis*) and tension (*Tensor veli palatini*; *N. trigeminus, otic ganglion*) of the soft palate. The upper constrictor presses (through the pterygo-pharyngeus) the posterior and lateral walls of the pharynx tightly against the posterior margin of the horizontal, tense, soft palate, whereby the margins of the posterior palatine arches (palato-pharyngeus) are approximated. The pharyngo-nasal cavity is thus completely shut off, so that the bolus cannot be pressed backwards into the nasal cavity (fig. 199 B).

In persons with congenital or acquired defects of the soft palate, or **cleft-palate**, during swallowing, food passes into the nose.

(6) *The food is prevented from passing into the larynx.* The bolus is propelled onwards by the successive contraction of the upper, middle, and lower constrictors of the pharynx until it passes into the œsophagus. At the same time the entrance to the glottis is closed, else the morsel would pass into the larynx, or, as is generally said, would "pass the wrong way."

Sounds during Deglutition.—If the region of the stomach be auscultated during the act of swallowing, two sounds may be heard; the first one is produced when the bolus is projected into the stomach; the second occurs when the peristalsis, which takes place at the end of swallowing, squeezes the contents of the œsophagus through the cardia (*Meltzer, Zenker, Ewald*). [The latter occurs a short time afterwards. In man, when water alone is swallowed, there is no sound, but when it is mixed with air there is, and it is generally heard because air is usually swallowed with the food or drink (*Quinke*).]

The **closure of the glottis** is effected in the following manner:—(a) The whole larynx—the lower jaw being fixed—is raised *upwards and forwards*, while at the same time the root of the tongue hangs over it. The hyoid bone is raised forwards and upwards by the genio-hyoid, anterior belly of the diaphragic, and mylo-hyoid; the larynx is approximated close to the hyoid bone by the thyro-hyoid. (b) When the larynx is raised, so that it comes to lie below the overhanging root of the tongue, the epiglottis is pressed downwards over the entrance to the glottis, and

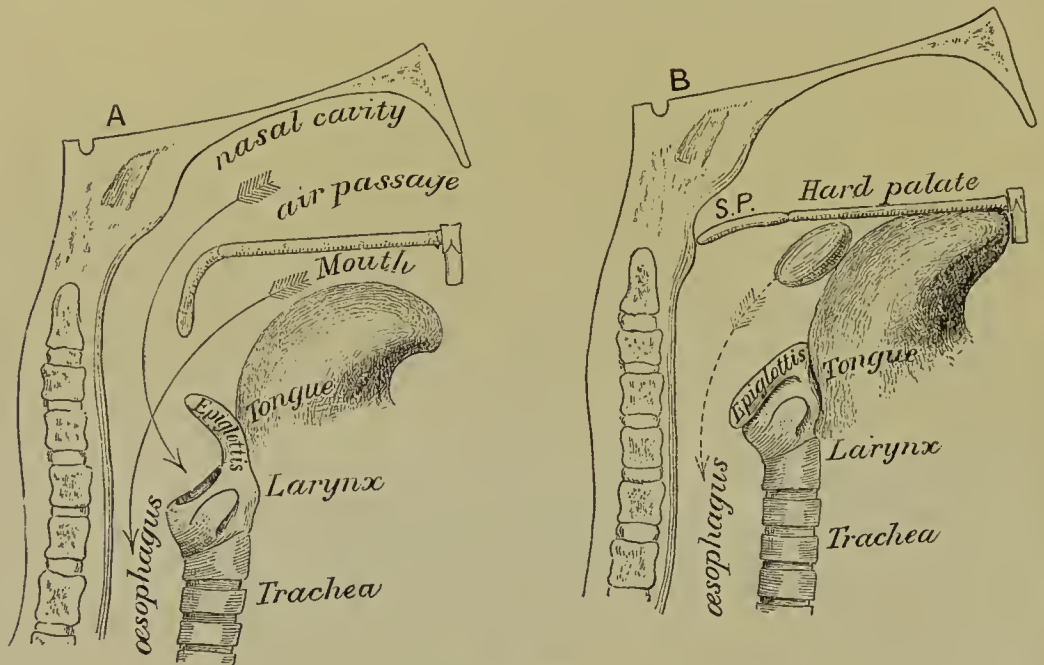


Fig. 199.

Scheme of deglutition.—A shows the passages and openings marked with arrows indicating the air- and food-channels. B, the act of deglutition.

the bolus passes over it. The epiglottis is also pulled down by the special muscular fibres of the reflector epiglottidis and aryepiglotticus. (c) The closure of the glottis by the constrictors of the larynx also prevents the entrance of substances into the larynx (§ 313, II. 2).

In order that the descending bolus may be prevented from carrying the pharynx with it, the stylo-pharyngeus, salpingo-pharyngeus, and baseo-pharyngeus contract upwards when the constrictors act.

Injury to the Epiglottis.—Intentional injury of the epiglottis in animals, or its destruction in man, may cause fluids to “go the wrong way,” *i.e.*, into the glottis, whilst solid food can be swallowed without disturbance. In dogs, coloured fluids placed on the root of the tongue have been observed to pass directly into the pharynx without coming into contact with it, so as to tinge the upper surface of the epiglottis (*Magendie*). [The basis of the epiglottis is yellow elastic cartilage, so that it shows no tendency to ossify, and always retains its elasticity (§ 313).]

[Experiments of Kronecker, Falk, and Meltzer. **Method.**—Meltzer placed in his œsophagus an œsophageal sound with a thin india-rubber bag tied to its lower end, and its upper end in con-

nection with a Marey's tambour. The sound was graduated into centimetres, so that by fixing it with the teeth, the depth to which the bag reached in the œsophagus could be ascertained at once. The elastic bag was inflated from a lateral tube so as to fill the œsophagus. The experiment was so arranged as to indicate the moment the act of swallowing commenced, a second bag being placed in the pharynx, and of course as the bolus—usually water—passed along the pharynx and œsophagus it compressed first the one and then the other bag, and a tracing was obtained of the relative time of passage.]

[In all experiments on deglutition it is important to remember that the size and consistence of the bolus cause different mechanisms to come into play. In swallowing water, for example, less than $\frac{1}{10}$ th second suffices to transport it from the mouth along the œsophagus. It is "projected," "shot-down" the œsophagus by the contractions chiefly of the muscles of the floor of the mouth—the mylo-hyoids—the œsophagus remaining open; and the œsophagus first contracts *after* the bolus is already in the stomach. If a large mass of considerable consistence is swallowed, this seems to require the help of the constrictors of the pharynx and the œsophageal walls.]

[From the tracing (fig. 200) it will be seen that the bolus—*e.g.*, water—is projected right into the stomach long before the œsophagus begins to contract. What Kronecker insists on is that in swallowing, say water or semi-fluid food, the food is not carried into the stomach by a complicated peristaltic act as described above; but that the act of deglutition is one act, due chiefly to the contraction of the mylo-hyoid muscles, which project the food right through the relaxed œsophagus into the stomach with considerable rapidity ($\frac{1}{10}$ sec.) and under a relatively high pressure. Of course at the same

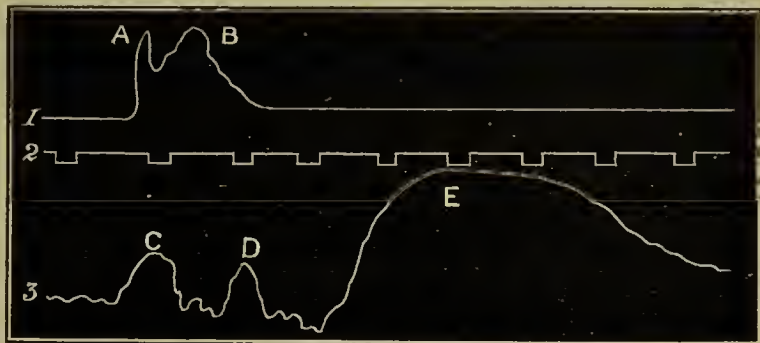


Fig. 200.

Tracing of the act of deglutition. 1, A indicates the compression of the elastic bag caused by the bolus projected by the contraction of the mylo-hyoid muscles; B, contraction of the pharynx, 2, Line marking seconds; 3, Tracing of the bag in the œsophagus 12 centimetres from the teeth; C, compression of the bag by the bolus corresponding to A; D, compression by the residues of the bolus carried on by the contraction of the pharynx, B; E, contraction of the œsophagus.

time the various side-openings to the posterior nares and entrance to the glottis have to be guarded and closed.]

[The mylo-hyoids form a hammock-like diaphragm, on which rests the tongue. There are also concerned the longitudinal and hyoglossi muscles; the latter pull the root of the tongue backwards and downwards.]

[When, however, the bolus is large and solid, then deglutition takes place much more slowly, and the bolus seems to meet with more resistance at certain parts in its passage, and to require the peristaltic action of the pharyngeal and œsophageal muscles to press it onwards.]

[Kronecker divides the digestive tube as far as the cardia into five muscular rings—1. Those for the first act, chiefly the mylo-hyoids. 2. The constrictors of the pharynx. 3. The first section of the œsophagus (cervical segment provided with striped muscle). 4. The upper dorsal segment of the œsophagus (partly striped and partly smooth muscle). 5. To the cardia (smooth muscle). In this connection we may recall the observation of Virchow in cases of poisoning by sulphuric acid, where he noticed that little effect was produced on the mouth or pharynx, the most marked effects of the action of the acid being at the entrance to the œsophagus where it crosses the left bronchus, and just before the cardia where it perforates the diaphragm.]

[Time relations.—As to the time relations of the contraction of the successive muscular rings we have the following:—

Contraction of mylo-hyoids and constrictor	0.3×1	Secs. = 0.3
“ “ first part of œsophagus	$0.3 \times (1 + 2)$	= 0.9
“ “ second “	$0.3 \times (1 + 2 + 3)$	= 1.8
“ “ third “	$0.3 \times (1 + 2 + 3 + 4)$	= 3.0
		6.0

i.e., if each part had to contract successively it would require at least 6 seconds before a bolus of food could be carried to the stomach, yet it is within the experience of all of us that the act occurs much more quickly. It will be seen that the above gives an arithmetical series of the second order with difference 1 and a constant factor 0.3.]

[It is necessary to distinguish a **single, isolated act of deglutition** from a **series**, or **succession** of these acts. If we make a series of acts of swallowing, as when we drink a glass of water, the œsophagus does not contract until *after* the last act of deglutition, and it contracts at the same interval of time after the beginning of the last act of deglutition as if only a single act had been carried out. It is obvious, therefore, that every act of swallowing not only excites an œsophageal contraction, but at the same time it inhibits the already excited but not yet manifested œsophageal contraction. Thus in swallowing a glass of water each successive act of deglutition inhibits the œsophageal contraction, so that the œsophagus remains open, and only contracts *after* the last drop of water is already in the stomach.]

Nervous Mechanism.—Deglutition is **voluntary** only during the time the bolus is in the mouth. When the food passes through the palatine arch into the gullet

the act becomes **involuntary**, and is, in fact, a well-regulated reflex action. When there is no bolus to be swallowed, voluntary movements of deglutition can be accomplished only within the mouth; the pharynx only takes up the movement, provided a bolus (food or saliva) mechanically excites the reflex act. The **afferent nerves**, which, when mechanically stimulated, excite the involuntary act of deglutition, are the palatine branches of the trigeminus (from the sphenopalatine ganglion and the pharyngeal branches of the vagus (fig. 201). [It can also be excited by stimulation of the central end of the superior laryngeal nerve.] The **centre** for the nerves concerned (for the striped muscles) lies in the superior olives of the medulla oblongata. Swallowing can be carried out when a person is unconscious, or after destruction of the cerebrum, cerebellum, and pons (§ 367, 6). [Even in the deep coma of alcoholism, the tube of a stomach-pump is carried into the stomach reflexly, provided the surgeon passes it back into the pharynx.] The nerves of the pharynx are derived from the **pharyngeal plexus**, which receives branches from the

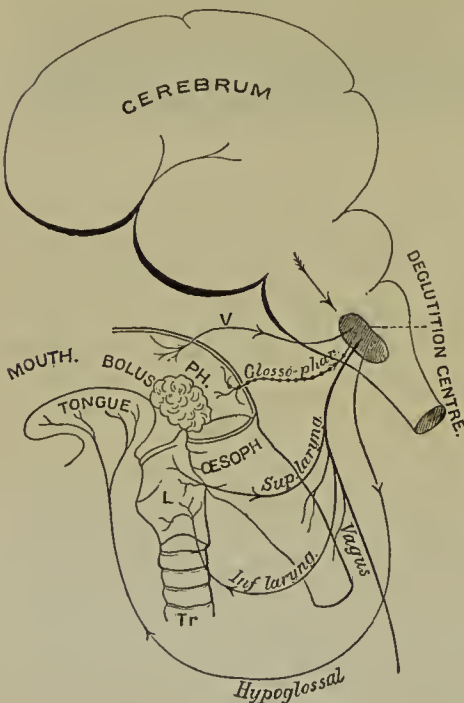


Fig. 201.

Scheme of the afferent and efferent nerves concerned in deglutition (*Stirling*).

vagus, glosso-pharyngeal, and sympathetic (§ 352, 4). Stimulation of the glosso-pharyngeal nerve inhibits reflex deglutition (*Kronecker and Vassilieff*).

[The efferent or motor nerves are those supplying the muscles concerned, (1) the *inferior maxillary division of the fifth cranial nerve* supplies the masseter, temporal, pterygoid, mylo-hyoid, and anterior belly of the digastric muscles; (2) the *facial* supplies the orbicularis oris, buccinator, stylo-hyoid, and posterior belly of the digastric; (3) the *hypoglossal* or ninth cranial nerve supplies the intrinsic muscles of the tongue, genio-hyoid, thyro-hyoid, genio-hyoglossus, hyoglossus, and stylo-glossus; (4) branches of the *pharyngeal plexus* (vagus, glosso-pharyngeal, and sympathetic) supply the constrictors of the pharynx, palato-glossus, and palato-pharyngeus; (5) a branch from the glosso-pharyngeal (?) supplies the stylo-pharyngeus; (6) the *facial* (petrosal) branch of the Vidian supplies the levator palati and azygos uvulae; (7) a branch from the otic ganglion of the fifth supplies the tensor palati; (8) the *inferior laryngeal branch of the vagus* supplies the muscles that close the glottis.]

[We have seen that the contraction of the œsophagus is inhibited during a succession of acts of deglutition. We know that the vagus conducts impulses which excite the œsophagus, and is therefore motor. Through the trigeminal reflex acts of deglutition can be excited. As to the glosso-pharyngeal, we know that its section does not set aside deglutition, nor does its stimulation excite the act of swallowing. The glosso-pharyngeal inhibits the occurrence of a reflex act of deglutition. If the glosso-pharyngeal be stimulated, the strongest stimuli to deglutition (*e.g.*, filling the pharynx with fluid, or stimulation of the superior laryngeal nerves) fail to discharge the act of deglutition; neither the first part of the act nor contraction of the œsophagus takes place. Stimulation of the lingual branch of the glosso-pharyngeal inhibits the first act of deglutition; while the pharyngeal branches seem to inhibit the œsophageal contractions, so that the **glosso-pharyngeal is the inhibitory nerve of deglutition.**]

[With each stimulus to the movement of the first act of deglutition (especially the mylo-hyoid group) there is an inhibition of the deeper sections through the stimulation of the glosso-pharyngeal nerve. This inhibition takes place in the nerve-centre in the medulla oblongata, for Mosso showed that the peristaltic movements of the œsophagus are propagated from above downwards, even after section of the œsophagus.]

[**Action on other Centres.**—The act of swallowing affects many other centres, *e.g.*, the cardio-motor in the medulla, it reduces the tonus of the heart vagus, so that the heart beats quicker (§ 369), it also affects the respiratory centre and diminishes the need for respiration, constituting “Deglutition-apnœa.” It also affects the vaso-motor and some other centres (*Kronecker*).]

[**Where the deglutition reflex is discharged.**—It is very difficult to determine from what parts of the mouth deglutition is excited. In the rabbit, by touching the anterior central part of the soft palate, a complete act of deglutition is discharged. This may be set aside by section of the trigeminal, or painting the part with cocaine. Parts of the larynx supplied by the superior laryngeal also excite it. In man the reflex is discharged when the bolus passes behind the velum in the region of the tonsils. Stimulation of the glosso-pharyngeal inhibits deglutition, but how it is caused is unknown. Stimulation of the pharynx, even muscular pressure, will inhibit it (*Wassilieff*).]

Within the **œsophagus**, whose stratified squamous epithelium is moistened with the mucus derived from the mucous glands in its walls, the downward movement is involuntary, and depends upon a complicated reflex movement discharged from the centre for deglutition. There is a peristaltic movement of the outer longitudinal and inner circular non-striped muscular fibres.

In the upper part of the œsophagus, which contains striped muscular fibres, the peristalsis takes place more quickly than in the lower part. The movements of the œsophagus never occur independently, but are always the continuation of a foregoing act of deglutition. If food be introduced into the œsophagus through a hole in its wall, there it lies; and it is only carried downwards when a movement to swallow is made. The peristalsis extends along the whole length of the œsophagus, even when it is ligatured or when a part of it is removed (*Mosso*). If a dog be allowed to swallow a piece of flesh tied to a string, so that the flesh goes half-way down the œsophagus, and if the flesh be withdrawn, the peristalsis still passes downwards (*C. Ludwig and Wild*).

The motor nerve of the œsophagus is the vagus (not the accessory fibres) [œsophageal, whose

branches have numerous small ganglia in their course]. After it is divided, the food lodges in the lower part of the œsophagus. Very large and very small masses are swallowed with more difficulty than those of moderate size. Dogs can swallow an olive-shaped body weighted with a counterpoise of 450 grams (*Mosso*). When the thorax is greatly distended, as in Müller's experiment, or greatly diminished, as in Valsalva's experiment (§ 60), deglutition is rendered more difficult.

Goltz's Experiments.—The œsophagus and stomach of the frog become more excitable, *i.e.*, the excitability of the ganglionic plexuses in their walls is increased, when the brain and spinal cord or both vagi are destroyed. These organs contract energetically after slight stimulation, while frogs, whose central nervous system is intact, swallow fluids simply by peristalsis. Females, and sometimes men also, suffering from hysteria, not unfrequently have similar spasmodic contractions of the œsophageal region (*globus hystericus*). After section of both vagi in the dog, Schiff observed spasmodic contraction of the œsophagus. [After section of the glosso-pharyngeal nerve the œsophagus may pass into a state of tonic spasm lasting about a day].

Effect on Circulation.—Every time one swallows, the heart's action is accelerated, the blood-pressure falls, the necessity for respiration diminishes, while many movements (labour pains, erection) tend to be inhibited. These effects are brought about reflexly (*Kronecker and Meltzer*, § 369).

[Structure of the Œsophagus.—The œsophagus in the dog and rabbit is almost entirely composed of striped muscle. In the cat and man, its upper part acts like a striped muscle, and its lower part is composed of smooth muscle. The œsophagus

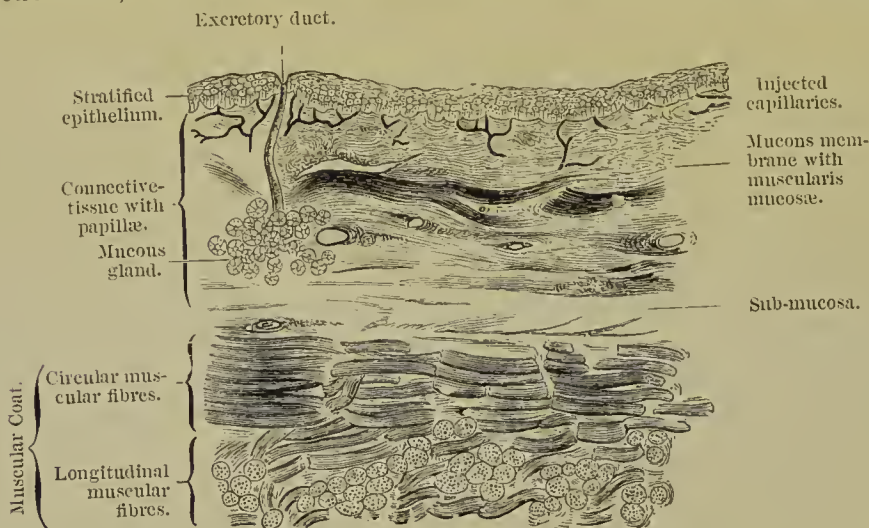


Fig. 202.

Transverse section of part of the œsophagus.

is almost 25 cm. long, and its walls are composed of **four coats**—mucous, sub-mucous, muscular, and fibrous (fig. 202).

(1) The **mucous coat** is firm, and is thrown into longitudinal folds, which disappear when the tube is distended. It is lined by several layers of **stratified squamous epithelium**. The membrane itself is composed, especially at its inner part, of dense fibrous tissue, which projects, in the form of **papillæ**, into the stratified epithelium. The papillæ are present in the child, but are largest in old people. At its outer part is a continuous longitudinal layer of non-striped muscle, the **muscularis mucosæ**. The layer consists of small bundles of non-striped muscle separate from each other.

(2) The **sub-mucous coat** is thicker than the foregoing, and consists of loose connective-tissue, with the acini of small mucous glands imbedded in it. The ducts pierce the muscularis mucosæ to open on the inner surface of the tube. Some animals have a considerable number of large mucous glands in the œsophagus (dog) and others have very few.

(3) The **muscular coat** consists of an **inner**, thicker, **circular**, and an **outer**, thinner, **longitudinal** layer of non-stripped muscle, commencing on a level with the cricoid cartilage. In man, the upper third of the gullet consists of striped muscular fibres.

(4) Outside the muscular coat is a layer of **fibrous tissue**,—the **adventitia**—with elastic fibres. The structure of the muscular coat of the œsophagus varies much in different animals. In the rabbit, in the first quarter of its length, it has two layers, but below this there are three layers, *i.e.*, a circular between an outer and an inner longitudinal layer, while the non-stripped fibres are confined to the lowest quarter of the tube.]

[**Nerve-Plexuses**.—As in the intestine, there are two plexuses of nerves with ganglia; one in the sub-mucous coat (*Meissner's*) and the other between the two muscular coats (*Auerbach's*), which are continuous with those in the stomach and intestine. Blood-vessels and numerous lymphatics lie in the mucous and sub-mucous coats.]

157. MOVEMENTS OF THE STOMACH.—Position.—When the stomach is empty, the great curvature is directed downwards and the lesser upwards; but when the organ is full, it rotates on an axis running horizontally through the pylorus and cardia, so that the great curvature appears to be directed to the front and the lesser backwards.

Arrangement of the Muscular Fibres.—The non-stripped muscular fibres of the stomach are arranged in three directions or layers. There is an outer **longitudinal** layer, whose fibres are continuous with those of the œsophagus and is best developed along the curvatures, especially the lesser. At the pylorus the fibres form a thick layer, and become continuous with the longitudinal fibres of the duodenum. The **circular** fibres form a complete layer; at the pylorus they are more numerous, and constitute the sphincter-muscle or **pyloric valve**; whilst at the cardia (inlet), such a muscular ring is absent. The innermost **oblique** or diagonal layer is incomplete.

The Movements of the Stomach are of two kinds:—The **rotatory** or **churning** movements, whereby the parts of the wall of the stomach in contact with the contents glide to and fro with a slow rubbing movement. Such movements seem to occur periodically, every period lasting several minutes (*Beaumont*). By these movements the contents are moistened with the gastric juice, while the masses of food are partly broken down. The formation of hair-balls in the stomach of dogs and oxen indicates that such rotatory movements of the contents of the stomach take place. (2) The other kind of movement consists in a periodically occurring **peristalsis**, whereby, as with a push, the first dissolved portions of the contents of the stomach are forced into the duodenum. They begin after a quarter of an hour, and recur until about five hours after a meal. This peristalsis is most pronounced towards the pyloric end, and the muscles of the pyloric sphincter relax to allow the contents to pass into the duodenum. According to Rüdinger, the longitudinal muscular fibres, when they contract, especially when the pyloric end is filled, may act so as to dilate the pylorus.

The following experiment is designed to determine the time at which the ingesta pass into the intestine. Salol splits up in an alkaline medium (in intestine) into phenol and salicylic acid, and the presence of the latter in the urine can be ascertained by ferric chloride (violet colour). In health the reaction begins in $\frac{1}{2}$ –1 hour, and disappears after 24 hours; in motor insufficiency of the stomach 3–24 hours later (*Huber*).

Gizzard.—The strongly muscular walls of the stomach of grain-eating birds effect a trituration of the food. The older physiologists found that glass balls and lead tubes, which could be compressed only by a weight of 40 kilos., were broken or compressed in the stomach of a turkey.

[**The nerves of the Stomach**.—It is supplied by nerve-fibres from the two **vagi** and the solar plexus. After forming the œsophageal plexus, the left vagus descends rather anterior to, and the right posterior to, the œsophagus, and they continue along it to the stomach. The left supplies chiefly the lesser curvature and the

anterior surface of the organ, together with branches to the liver, and, perhaps the duodenum, while the right gives branches to the posterior surface of the stomach, about two-thirds of its fibres passing to the solar plexus. The gastric branches of the vagus contain for the most part non-medullated fibres.]

[From the solar or **celiac plexus** branches—chiefly composed of non-medullated fibres—proceed, constituting the **gastric plexus** of the splanchnic nerves along the gastric artery to the stomach, where they intermingle with the branches from the vagi under the peritoneal covering. Small ganglia exist in the course of these nerves. Branches penetrate the coats of the stomach along with the arteries, and, between the longitudinal and circular muscular coats, form **Auerbach's plexus**, and **Meissner's plexus** in the sub-mucous coat.]

[Branches from Meissner's plexus pass to the mucous membrane, some to supply the muscularis mucosæ, and it may be to the glands as well, but this latter point has not been proved histologically.]

Influence of Nerves on the Stomach.—**Auerbach's ganglionic plexus** of nerve-fibres and nerve-cells, which lies between the muscular coats of the stomach, must be regarded as its proper motor centre, and to it motor impulses are conducted by the vagi. **Section of both vagi** does not abolish, but it diminishes the movements of the stomach. The muscular fibres of the cardia may be excited to action, or their action inhibited by fibres which run in the vagus (Nn. constrictores, et dilatator cardiae). [If the vagi be divided in the neck, there is a short temporary spasmodic contraction of the cardiac aperture. On stimulating the peripheral end of the vagus with electricity, after a latent period of a few seconds, the cardiac end contracts, more especially if the stomach be distended, but the movements are slight if the stomach be empty. In curarised dogs, the **pylorus** contracts with varying intensity, and irregularly, whether the vagi and splanchnics be intact or divided. Stimulation of the vagi in the neck causes contraction of the pylorus, when the latent period may be seven seconds. Stimulation of the splanchnics in the thorax arrests the spontaneous pyloric contractions, the left splanchnic being more active than the right (*Oser*).]

In the cardia are **automatic ganglionic cells** (analogous to the cardiac ganglia), which are connected with the vagus and sympathetic. [They lie in groups (11 in the rabbit) and are not to be confounded with Auerbach's plexus.] A centre for the contraction of the cardia lies in the posterior pair of the corpora quadrigemina; the efferent channels for the impulses seem to be through the vagi and partly through the splanchnics. The centre for the opening of the cardia, [*i.e.*, the origin of the dilator cardiae] lies in the anterior inferior end of the corpus striatum, and the conducting paths in the vagi. The cardia may be opened reflexly by stimulation of the sensory abdominal nerves [*e.g.*, of the kidney, uterus, intestine].

The body of the stomach also possesses a few **automatic ganglia** in connection with the vagi and sympathetic. A centre for its contraction lies in the corpora quadrigemina, and the efferent paths lie in the vagi but chiefly in the cord, and from the latter into the sympathetic. Inhibitory centres lie in the upper part of the cord, and the efferent paths are in the sympathetic and splanchnics.

The **pylorus** also contains **automatic centres**. The centre for opening the cardia inhibits the movement of the pylorus, the path being through the cord and splanchnics. Inhibitory pyloric centres lie in the corpora quadrigemina and olives, the paths are in the cord. The centres in the cortex [sulcus cruciatus] for opening the cardia at the same time contract the pylorus. The contraction-centres for the pylorus lie in the corpora quadrigemina (*Openchowski*). [These results refer to the dog and rabbit.]

Local electrical stimulation of the surface of the stomach causes circular constrictions of the organ, which disappear very gradually, while the movement is often propagated to other parts of the gastric wall. When heated to 25° C., the excised empty stomach exhibits movements. Injury to the pedunculi cerebri, optic thalamus, medulla oblongata, and even to the cervical part of the spinal cord, according to Schiff, causes paralysis of the vessels of certain areas of the stomach, resulting in congestion and subsequent hæmorrhage into the mucous membrane. [It is no uncommon occurrence to find hæmorrhage into the gastric mucous membrane of rabbits, after they have been killed by a violent blow on the head.]

Action of Drugs.—The **automatic centres** are excited by emetin, apomorphin, tartar emetic, while muscarin causes general contraction of the stomach. The activity of the auto-

matic centres is diminished by chloral, urethan, morphin, and nicotin, while atropin causes paralysis of the nerve-endings (*E. Schütz*).]

158. VOMITING.—Mechanism.—Vomiting is caused by contraction of the walls of the stomach, the pyloric sphincter being closed. It occurs most readily when the stomach is distended—(dogs usually greatly distend the stomach by swallowing air before they vomit); it readily occurs in infants, in whom the cul-de-sac at the cardia is not developed. It is quite certain that in children vomiting occurs through contraction of the walls of the stomach, without the spasmodic action of the abdominal walls. When vomiting is violent, the abdominal muscles act energetically. [The act of vomiting is generally preceded by a feeling of nausea, and usually there is a rush of saliva into the mouth, caused by a reflex stimulation of afferent fibres in the gastric branches of the vagus, the efferent nerve for the secretion of saliva being the chorda tympani. After this a deep inspiration is taken, and the glottis closed, so that the diaphragm is firmly pressed downwards against the abdominal contents, and it is kept contracted; the lower ribs are pulled in. The diaphragm being kept contracted and the glottis closed, a violent expiratory effort is made, so that the contraction of the abdominal muscles acts upon the abdominal contents, the stomach being forcibly compressed. The cardiac orifice is opened at the same time, and the contents of the stomach are ejected. The chief agent seems to be the abdominal compression, but the walls of the stomach also help, though only to a slight extent.]

The contraction of the walls of the stomach, which causes a general diminution of the gastric cavity, is not a true anti-peristalsis, as can be seen in the stomach when it is exposed. The *cardia is opened* by the longitudinal muscular fibres, which pull towards the lower orifice of the œsophagus, so that when the stomach is full they must act as dilators. The act of vomiting is preceded by a ractus-like dilating movement of the intra-thoracic part of the œsophagus, which is caused thus: The glottis is closed, inspiration occurs suddenly and violently, whereby the œsophagus is distended by gases proceeding from the stomach. The larynx and hyoid bone, by the combined action of the genio-hyoid, sterno-hyoid, sterno-thyroid, and thyro-hyoid muscles, are forcibly pulled forwards, so that the air passes from the pharynx downwards into the upper section of the œsophagus. If the abdominal walls contract suddenly, and if this sudden impulse be aided by the movements of the stomach itself, the contents of the stomach are forced outwards. During continued vomiting, antiperistalsis of the duodenum may occur, whereby bile passes into the stomach, and becomes mixed with its contents.

Children, in whom the fundus is absent, vomit more easily than adults. [In them also the nervous system is more excitable.]

Influence of Nerves.—The **centre** for the movements concerned in vomiting lies in the medulla oblongata, and is in relation with the respiratory centre, as is shown by the fact that nausea may be overcome by rapid and deep respirations. In animals, vomiting may be inhibited by vigorous artificial respiration. On the other hand, the administration of certain emetics prevents the occurrence of apnoea.

In vomiting, the **afferent impulses** may be discharged from (1) the mucous membrane of the soft palate, pharynx, root of the tongue (*glosso-pharyngeal nerve*), as in tickling the fauces with the finger; (2) the nerves of the stomach (*vagus* and *sympathetic*); (3) stimulation of the uterine nerves (pregnancy); (4) the *mesenteric* nerves (inflammation of the abdomen and hernia); (5) nerves of the urinary apparatus (passing a renal calculus); (6) nerves to the liver and gall-duct (*vagus*); (7) nerves to the lungs in phthisis (*vagus*). Vomiting is also produced by *direct* stimulation of the vomiting centre. [The **efferent impulses** are carried by the phrenics (diaphragm), vagus (œsophagus and stomach), and intercostals (abdominal muscles).]

Vomiting, produced by the thought of something disagreeable, appears to be caused by the conduction of the excitement from the cerebrum to the vomiting centre. [It may also be excited through the *brain* by a disagreeable smell, shocking sight, or by other impressions on the nerves of special sense.] Vomiting is very common in diseases of the brain [tubercle,

inflammation, hæmorrhage.] Section of both vagi generally, but not always, prevents vomiting.

Emetics act (1) partly by mechanically or chemically stimulating the ends of the centripetal (afferent) nerves of the mucous membrane. [These are *local* emetics.] Tickling the fauces, touching the surface of the exposed stomach (dog); and many chemical emetics, *e.g.*, mustard, cupric and zinc sulphate, and other metallic salts, act in this way. (2) Other substances cause vomiting when they are introduced into the blood (without being first introduced into the stomach), and act directly upon the vomiting centre, *e.g.*, apomorphin. [These are *general* emetics.] (3) Lastly, there are some substances which act in both ways, *e.g.*, tartar emetic. Emetics may also remove mucus from the lungs, and in this case it is probable that the emetic acts upon the respiratory centre, and so favours the respirations. The *general* emetics usually create considerable depression, while the vomiting lasts longer than with local emetics. The former increase the salivary, gastric, and respiratory secretions.

Uses of Emetics.—Emetics are useful not only for removing from the stomach any offending body, be it a poison or the products of imperfect or perverted gastric digestion, or bile which has passed back into the stomach, but foreign bodies impacted in the œsophagus may be got rid of on exciting vomiting by the subcutaneous injection of apomorphin. As the diaphragm contracts vigorously during vomiting, it compresses the liver, and thus bile is expelled into the duodenum, or the passage of a small calculus along the bile-duct may be aided. They also are useful in removing mucus or false membranes from the respiratory passages.]

[Anti-Emetics.—Vomiting may be allayed by *local* anti-emetics such as ice, and many chemical substances such as bismuth, hydrocyanic acid, opium, and morphia, as well as by *general* remedies which act on the vomiting centre. Some of the foregoing drugs perhaps act both locally and generally.]

Vomiting is analogous to the process of rumination in animals that chew the cud (§ 187). Some persons can empty their stomachs in this way.

159. Movements of the intestine.—[The intestines consist of the *small* and *large intestine*; the *small intestine* commences at the pylorus and ends at the junction of the ileum with the large intestine (*i.e.*, at the cæcum), and its length is about $6\frac{3}{4}$ metres (about 20 feet) (fig. 172).]

[The first part of the *small intestine* is the *duodenum*, about 22 cm. long and 5 cm. in diameter; of the remainder the upper third is called the *jejunum* (2·2 metres long) and the lower two-thirds the *ileum* (about 4 metres long), but there is no line of demarcation between these parts, the one shading into the other. The *large intestine* is about 1·4–1·8 metres long (about 5 feet), wider than the small and extends from the termination of the ileum to the anus. It is divided anatomically into the *cæcum* with the vermiform appendix, the *colon*, and the *rectum*.]

[Comparative length and capacity of the intestines.—There is a marked difference between the intestinal canal of herbivora and carnivora. Vegetable food requires a much larger number of mechanical and chemical aids for its digestion than animal food. The intestinal canal is shortest in carnivora (cat, lion, dog), longer in omnivora (man, apes), and longest, sometimes very long, and with enormous dilatations, in the pure herbivora. In the tiger and lion the whole digestive tract is 3 times as long as the body (*i.e.*, from the nose to the anus); in the dog, 5; chimpanzee, 6; man, 9 times. In herbivora it is 11–26 times as long as the body; horse, 12 times; pig, 16; ox, 20; and goat 26 times. The intestinal canal of the horse is comparatively short, but its capacity is very great. The capacity of the intestinal tract (excluding the stomach) is in the ox, 80 litres; horse, 200; pig, 27; and dog 8. The capacity of the stomach in the ox is 200, and in the horse only 10–18 litres. The superficial area of the intestinal mucous membrane is in the ox, 15; horse, 15–51; pig, 3, and dog, 0·5 square metres (*Munk*).]

Peristalsis.—The best example of peristaltic movements is afforded by the small intestine; the progressive narrowing of the tube proceeds from above downwards, thus propelling the contents before it. Frequently after death, or when air acts freely upon the gut, the peristalsis develops at various parts of the intestine simultaneously, whereby the loops of intestine present the appearance of a heap of worms ereeping amongst each other. The advance of new intestinal contents again increases the movement. In the large intestine the movements are more sluggish and less extensive. The peristaltic movements may be seen and felt when the abdominal walls are very thin, and also in hernial sacs. They are more lively in vegetable feeders than in carnivora. The peristalsis is perhaps conducted directly through the muscular substance itself, as in the heart and ureter. The movements of the stomach and intestine cease during sleep (*Busch*).

[**Rate of Motion.**—In a Thiry-Velly fistula (§ 183, II.) Fubini estimated the rate of motion of a smooth sphere of sealing-wax along the intestine. It took 55 sec. to travel 1 cm. [$\frac{2}{3}$ in.]; an induction-current greatly increases the motion, to 1 cm. in 10 seconds; NaCl does not affect it, but excites secretion; laudanum paralyzes it.]

[**Method of Observation.**—Open the abdomen of an animal under a .6 per cent. saline solution to prevent the exposure of the gut to air (*Saunders and Braam-Houckgeest*).

The **ileo-colic valve**, as a rule, prevents the contents of the large intestine from passing backwards into the small intestine.

When fluid is slowly introduced into the rectum through a tube, it passes upwards into the intestine, and even goes through the ileo-colic valve into the small intestine. Muscarin excites very lively peristalsis of the intestines, which may be set aside by atropin (*Schmiedeberg and Koppe*).

Pathological.—When any condition excites an acute inflammation of the intestinal mucous membrane, catarrh is rapidly produced, and very strong contractions of the inflamed parts filled with food take place. When these parts of the gut become empty, the movements are not stronger than normal. If new material passes into the inflamed part, the peristalsis recurs, becomes more lively than normal, and the result is diarrhœa (*Nothnagel*). Sometimes a greatly contracted part of the small intestine is pushed into the piece of gut directly continuous with it, giving rise to **invagination**, or **intussusception**.

Anti-peristalsis, *i.e.*, a movement which travels in an upward direction towards the stomach, does not occur normally. This has been inferred from the fact, that in cases where the intestine is occluded, called **ileus**, fæcal matter is vomited. Nothnagel's experiments throw doubts upon this view, as he failed to observe anti-peristalsis in cases where the intestine was occluded artificially. The fæcal odour of the ejecta may result from the prolonged retention of the material within the small intestine.

160. EXCRETION OF FÆCAL MATTER.—The contents of the small intestine remain in it about three hours, and about twelve hours in the large intestine, where they become less watery, and they assume the characters of fæces, become "formed" in the lower part of the great intestine. The fæces are gradually carried along by the peristaltic movement, until they reach a point a little above that part of the rectum which is surrounded by both sphincters, the internal sphincter consisting of non-striped, and the external of striped muscle.

Immediately after the expulsion of the fæces the external sphincter (fig. 203, S, and fig. 204) usually contracts vigorously, and remains so for some time. Afterwards it relaxes, when the elasticity of the parts surrounding the anal opening, particularly of the two sphincters, suffices to keep the anus closed. In the interval between two evacuations there does not seem to be a continued tonic contraction of the sphincters. As long as the fæces lie above the rectum, they do not excite any conscious sensations, but the sensation of requiring to go to stool occurs when the fæces pass into the rectum. At the same time, the stimulation of the sensory nerves of the rectum causes a reflex excitement of the sphincters. The centre for these movements (*Budge's centrum anospinale*) lies in the lumbar region of the spinal cord (§ 362); in the rabbit between the sixth and seventh, and in the dog at the fifth lumbar vertebra (*Masius*).

In animals whose spinal cord is divided above the centre, a slight touch in the region of the anus causes this orifice to contract, but after this lively reflex contraction the sphincters relax again, and the anus may remain open for a time. This occurs because the voluntary impulses which proceed from the brain to cause the contraction of the external sphincter are absent.

Landois observed that in dogs with the posterior roots of their lower lumbar and sacral nerves divided, the anus remained open, and not unfrequently a mass of fæces remained half ejected. As the sensibility of the rectum and anus was abolished in these animals, the sphincters could not contract reflexly, nor could there be any voluntary contraction of the sphincters, the result of sensory impulses from the rectum.

The external sphincter can be contracted *voluntarily*, like any voluntary muscle, but the closure of the anus can only be effected up to a certain degree. When the pressure from above is very great, the energetic peristalsis at last overcomes

the strongest voluntary impulses. Stimulation of the peduncles of the cerebrum and of the spinal cord below this point causes contraction of the external sphincter.

Defæcation.—The evacuation of the fæces, which in man usually occurs at certain times, begins with a lively peristalsis of the large intestine, which passes downwards to the rectum. In order that the mass of fæces may not excite reflexly the sphincter-muscles, in consequence of mechanical stimulation of the sensory nerves of the rectum, there seems to be a centre which **inhibits** the reflex action of the sphincters, which is called into play, owing, as it appears, to voluntary

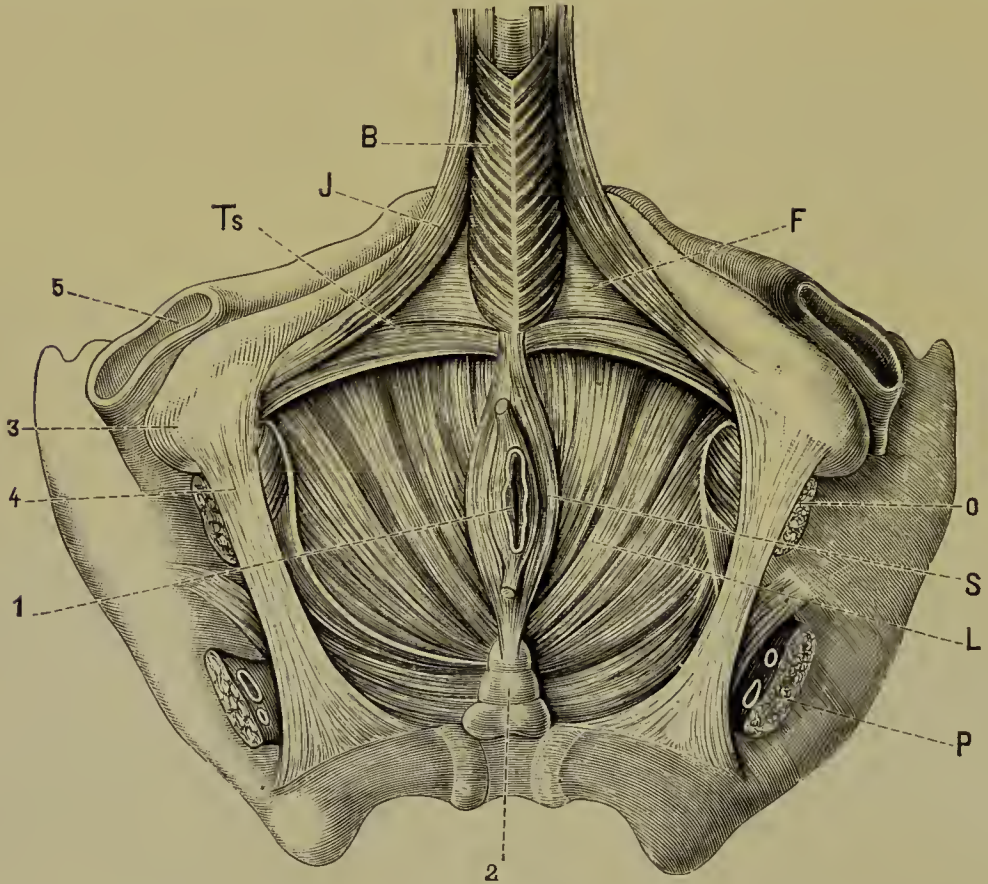


Fig. 203.

The perinaeum and its muscles. 1, anus; 2, coccyx; 3, tuberosity; 4, sciatic ligament; 5, cotyloid cavity; B, bulbo-cavernosus muscle; Ts, superficial transverse perineal muscle; F, fascia of the deep transverse perineal muscle; J, ischio-cavernosus muscle; M, obturator internus; S, external anal sphincter; L, levator ani; P, pyriformis.

impulses. Its seat is in the brain, perhaps in the optic thalami. When this inhibitory apparatus is in action, the fæcal mass passes through the anus, without causing it to close reflexly. The strong peristalsis which precedes defæcation can be aided, and to a certain degree excited by rapid voluntary movements of the external sphincter and levator ani, whereby the plexus myentericus of the large intestine is stimulated mechanically, thus causing lively peristaltic movements in the large intestine. The expulsion of the fæces is also aided by the pressure of the abdominal muscles, and most efficiently when a deep respiration is taken, so as to fix the diaphragm, whereby the abdominal cavity is diminished to the greatest extent. The soft parts of the floor of the pelvis, during a strong effort at stool, are driven downwards in the form of a cone, causing the mucous membrane

of the anus, which contains much venous blood, to be everted. The function of the levator ani (figs. 203, 204) is to raise voluntarily the soft parts of the floor of the pelvis, and to pull the anus to a certain extent upwards over the descending faecal mass. At the same time, it prevents the distention of the pelvic fascia. As the fibres of both levatores converge below, and become united with the fibres of the external sphincter, they aid the latter during energetic contraction of the sphincter; or, as Hyrtl put it, the levatores are related to the anus, like the two cords of a tobacco pouch. During the periods between the evacuation of the gut,

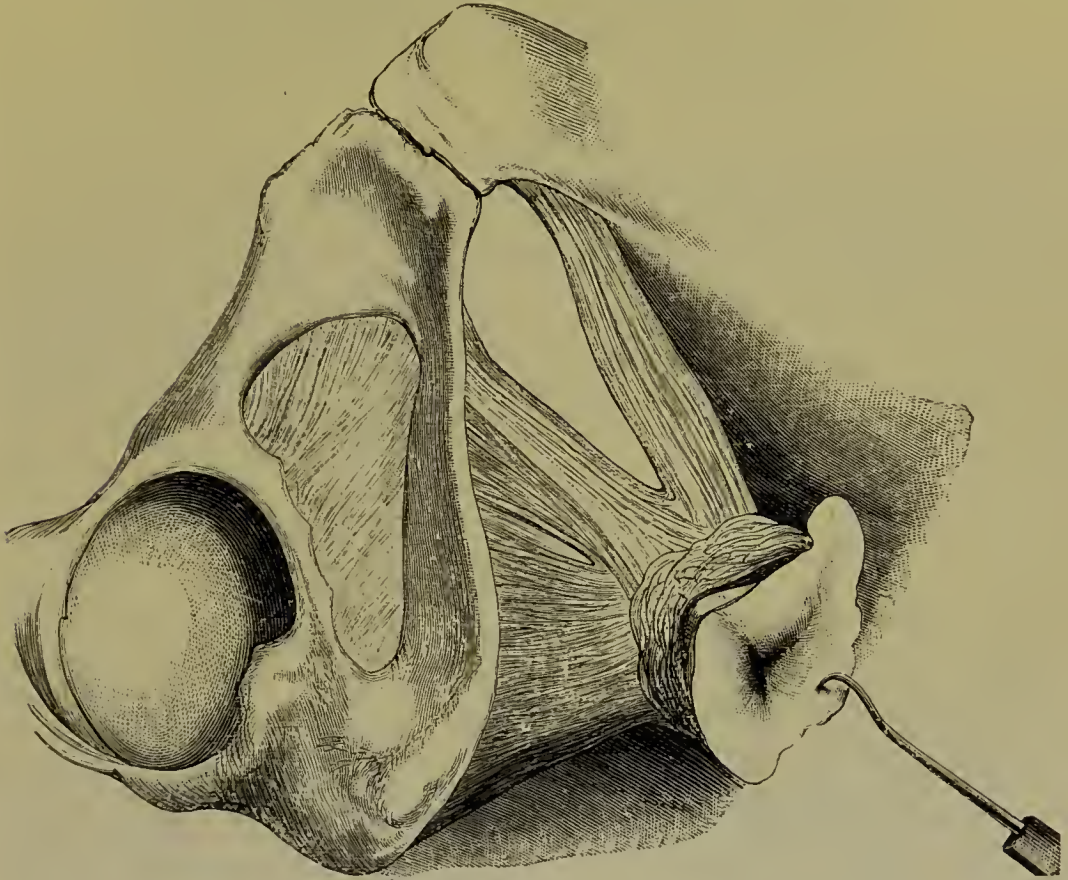


Fig. 204.

Levator ani and sphincter ani externus.

the faeces appear only to reach the lower end of the sigmoid flexure. As a rule, from thence downwards, the rectum is normally devoid of faeces. It seems that the strong circular fibres of the muscular coat, which Nélaton has called sphincter ani tertius, when they are well developed, contract, and prevent the entrance of the faeces. When the tendency to the evacuation of the rectum is very pressing, the anus may be closed more firmly from without, by energetically rotating the thigh outwards, and contracting the muscles of the gluteal region.

161. CONDITIONS INFLUENCING THE INTESTINAL MOVEMENTS.—

The intestinal canal contains **automatic motor centres** within its walls,—the **plexus myentericus** of Auerbach—which lies between the longitudinal and circular muscular fibres of the gut. It is this plexus which enables the intestine, when cut out of the body, to execute, apparently spontaneously, movements for some time.

[Structure.—Auerbach's Plexus consists of non-medullated nerve-fibres which form a fairly dense network, groups of ganglion cells occurring at the nodes (fig. 206, and when seen in vertical sections between the muscular coats it is like fig. 205. A similar plexus extends throughout the whole intestine between the longitudinal and circular muscular coats from the cesophagus to the rectum. Branches are given off to the muscular bundles. A similar, but



Fig. 205.

Auerbach's plexus shown in section (human). *a*, ganglionic cells; *b*, nerve fibres; *c*, section of the circular muscular fibres; *d*, longitudinal muscular fibres.

not so rich a plexus, lies in the sub-mucous coat—Meissner's plexus—which gives branches to supply the muscularis mucosæ, the smooth muscular fibres of the villi, and the glands of the intestine (fig. 207).]

1. If this centre is not affected by any stimulus, the movements of the intestine cease—comparable to the condition of the medulla oblongata in apnoea. The same is true—just as in the case of the respiration—during intra-uterine life, in consequence of the foetal blood being well supplied with O. This condition may be

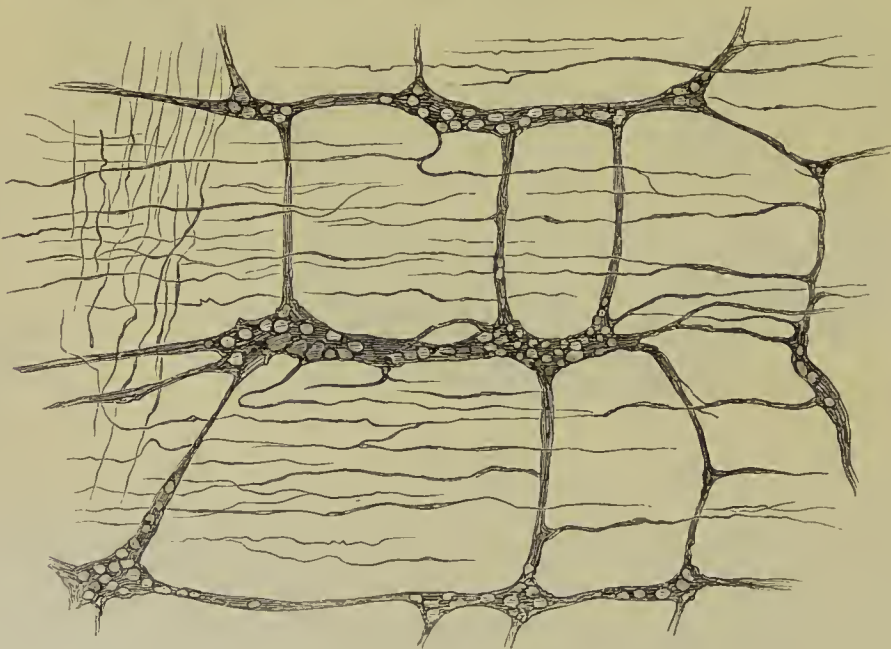


Fig. 206.

Plexus of Auerbach, prepared from the small intestine of a dog, by the action of gold chloride. The nerve-cells are shown at the nodes, while the fibrils proceeding from the ganglia, and the anastomosing fibres, lie between the muscular bundles.

termed **aperistalsis**. It also occurs during sleep, perhaps on account of the greater amount of O in the blood during that state.

2. When blood containing the normal amount of blood-gases passes through the intestinal blood-vessels, the quiet peristaltic movements of health occur (**euperistalsis**) provided no other stimulus be applied to the intestine.

3. All stimuli applied to the plexus myentericus increase the peristalsis, which may become so very violent as to cause evacuation of the contents of the large gut, and may even produce spasmodic contraction of the musculature of the intestine. This condition may be termed **dysperistalsis**, corresponding to dyspnœa. The condition of the blood flowing through the intestinal vessels affects the peristalsis.

Condition of the Blood.—**Dysperistalsis** may be produced by (a) interrupting the circulation of the blood in the intestines, no matter whether anæmia (as after compressing the aorta—*Schiff*) or venous hyperæmia be produced. The stimulating condition is the want of O, *i.e.*, the increase of CO₂. Very slight disturbance in the intestinal blood-vessels, *e.g.*, venous congestion after copious transfusion into the veins, whereby the abdominal and portal veins become congested, causes increased peristalsis. The intestines become nodulated at one part and narrow at another, and involuntary evacuation of the fæces takes place when there is congestion, owing to the plugging of the intestinal blood-vessels when blood from another species of animal is used for transfusion (§ 102). The marked peristalsis which occurs on the approach of death is undoubtedly due to the derangements of the circulation, and the consequent alteration of the amount of gases in the blood of the intestine. The same is true of the increased movements of the intestines which occur as a result of psychical excitement, *e.g.*, grief. The stimulus, in this case, passes from the cerebrum through the medulla oblongata (vaso-motor centre) to the intestinal nerves, and causes anæmia of the intestine (corresponding to the pallor occurring elsewhere). When the normal condition of the circulation is restored, the peristalsis diminishes. (b) Direct stimulation of the intestine, conducted to the plexus myentericus, causes *dysperistalsis*; direct exposure of the intestines to the air (stronger when CO₂ or Cl is present)—introduction of various irritating substances into the intestine—increased filling of the intestine when there is any difficulty in emptying the gut (often in man)—direct stimulation of various kinds (also inflammation),—all act upon the intestine, either from without or from within. Induction-shocks applied to a loop of intestine in a hernial sac cause lively peristalsis in the hernia. With increasing heat, at first there is diminished movement or cessation of movement (stimulation of the splanchnics); on heating to 43° the movements recommence.

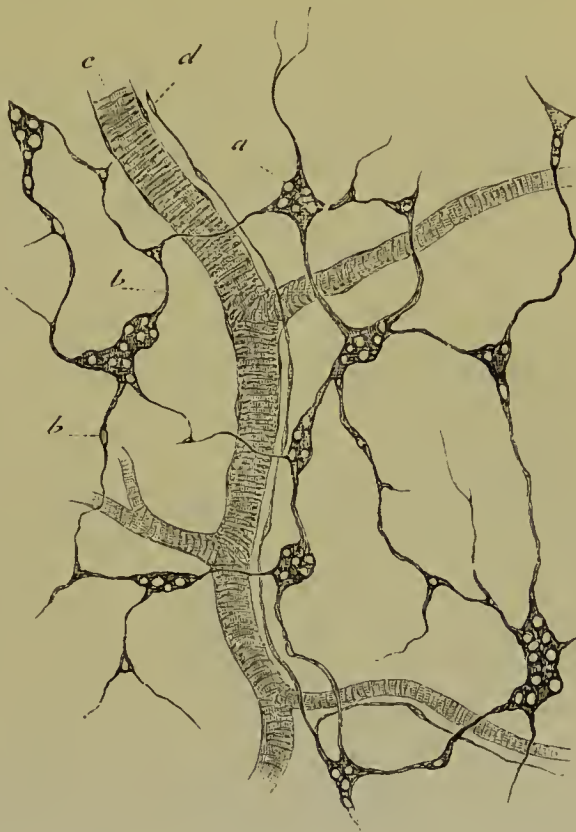


Fig. 207.

Plexus of Meissner. *a*, ganglia; *b*, anastomosing fibres; *c*, artery; *d*, vaso-motor nerve-fibres accompanying *c*.

4. The continued application of strong stimuli causes the dysperistalsis to give place to rest, owing to over-stimulation, which may be called "**intestinal paresis**," or exhaustion.

This condition is absolutely different from the passive condition of the intestine in aperistalsis. Continued congestion of the intestinal blood-vessels ultimately causes intestinal paralysis, *e.g.*, when transfusion of foreign blood causes coagulation within these vessels. Filling the blood-vessels with "indifferent" fluids, after the peristalsis has been previously brought about by compressing the aorta, also causes cessation of the movements (*O. Nasse*). The movements cease when the intestines are cooled to 19° C. (*Horwath*), while severe inflammation of the intestine has a similar effect. Under favourable circumstances, the intestine may recover from

this condition. Arterial blood admitted into the vessels of the exhausted intestine causes peristalsis, which at first is more vigorous than normal.

5. The continued application of strong stimuli causes **complete paralysis** of the intestine, such as occurs after violent peritonitis, or inflammation of the musculature or mucous coat in man. In this condition the intestine is greatly distended, as the paralysed musculature does not offer sufficient resistance to the intestinal gases which are expanded by the heat. This constitutes the condition of **meteorism**.

Influence of Nerves.—With regard to the nerves of the intestine, stimulation of the **vagus** increases the movements (of the small intestine), either by conducting impressions to the plexus myentericus, or by causing contraction of the stomach, which stimulates the intestine in a purely mechanical manner (*Braam-Houckgeest*). The **splanchnic** is (1) the **inhibitory** nerve of the small intestine (*Pflüger*), but only as long as the circulation in the intestinal blood-vessels is undisturbed, and the blood in the capillaries does not become venous; when the latter condition occurs, stimulation of the splanchnic increases the peristalsis. If arterial blood be freely supplied, the inhibitory action continues for some time. Stimulation of the origin of the splanchnics, of the spinal cord in the dorsal region (under the same conditions), and even when general tetanus has been produced by the administration of strychnia, causes an inhibitory effect. It is inferred that the splanchnic contains besides inhibitory fibres—which are easily exhausted by a venous condition of the blood, also (2) **motor fibres**, which remain excitable for a longer time, because after death stimulation of the splanchnics always causes peristalsis, just like stimulation of the vagus. (3) It is the **vaso-motor nerve** of the intestinal blood-vessels, so that it governs the largest vascular area in the body. When it is stimulated, all the vessels of the intestine which contain muscular fibres in their walls contract; when it is divided, they dilate. In the latter case, a large amount of blood accumulates within the blood-vessels of the abdomen, so that there is anæmia of the other parts of the body, which may be so great as to cause death—owing to the deficient supply of blood to the medulla oblongata. (4) It is the **sensory nerve** of the intestine, and, under certain circumstances, it may give rise to very painful sensations.

As stimulation of the splanchnic contracts the blood-vessels von Basch has raised the question whether the intestine does not come to rest, owing to the want of the blood, which acts as a stimulus. But, when a weak stimulus is applied to the splanchnic, the intestine ceases to move before the blood-vessels contract (*van Braam-Houckgeest*); it would therefore seem that the stimulation diminishes the excitability of the plexus myentericus. According to Engelmann and v. Brakel, the peristaltic movement is chiefly propagated by direct muscular conduction, as in the heart and nreter, without the intervention of any nerve-fibres.

Effect of Nerves on the Rectum.—The *nervi erigentes*, when stimulated, cause the longitudinal muscular fibres of the rectum to contract, while the circular muscular fibres are supplied by the hypogastric nerves. Stimulation of the latter nerves also exerts an inhibitory effect on the longitudinal muscles. Stimulation of the *nervi erigentes* inhibits not only the spontaneous movements of the circular fibres of the rectum, but also those movements excited by stimulation of the hypogastric nerves (*Fellner*).]

[Artificial Circulation in the Intestine.]—Ludwig and Salvioli excised a loop of intestine from an animal, tied a cannula into an artery and another into a vein, and kept it in a warm moist atmosphere. The arterial cannula was connected with a vessel containing defibrinated blood, to which different drugs could be added. A lever rested on the intestine, and registered its movements on a recording surface. As long as arterial blood was transfused, the intestine was nearly quiescent, but when it was arrested, so that the blood became *venous*, a series of contractions occurred. *Nicotin* diminished the flow of blood and quickened the intestinal movements, while at the same time the circular muscular fibres remained contracted or tetanic. *Tincture of opium*, in the proportion of .01 to .04 in the blood, causes at first contraction of the vessels, and lessens the amount of blood circulating in the intestine; but it very rapidly increases—even to six times—the amount of blood which transfuses, while at the same time the movements of the intestine cease, the walls of the intestine being contracted. *Peptone* caused first strong and then irregular contractions.]

Effect of Drugs.—Amongst the reagents which act upon the intestinal movements are:—(1) Such as diminish the excitability of the plexus myentericus, *i.e.*, which lessen or even abolish

intestinal peristalsis, *e.g.*, belladonna. (2) Such as stimulate the inhibitory fibres of the splanchnic, and in large doses paralyse them—opium, morphia; 1 and 2 produce constipation. (3) Other agents excite the motor apparatus—nicotin (even causing spasm of the intestine), muscarin, caffein, and many laxatives, which act as purgatives. The movements produced by muscarin are abolished by atropin. These substances accelerate the evacuation of the intestine, and, owing to the rapid movement of the intestinal contents, only a small amount of water is absorbed; so that the evacuations are frequently fluid. (4) Amongst *purgatives*, colocynth and croton oil act as direct irritants. With regard to drugs of this sort, they seem to cause a watery transudation into the intestine, just as croton oil causes vesicles when applied to the skin. (5) Calomel is said to limit the absorptive activity of the intestinal wall, and to control the decompositions in the intestine. The stools are thin and greenish, from the admixture of biliverdin. (6) Certain saline purgatives—sodium sulphate, magnesium sulphate—cause fluid evacuations by retaining the water in the intestine; and it is said that if they be injected into the blood-vessels of animals, they cause constipation. [When a crystal of a *potash salt* is applied to the peritoneal surface of the intestine of an animal, it causes merely a local constriction of the muscular fibres of the gut, while a *sodium salt* excites a contraction which passes upwards towards the stomach, and never towards the rectum. In any case it may serve as a useful guide to the surgeon, in determining which is the upper end of a piece of intestine during an operation on the intestines (*Nothnagel*).]

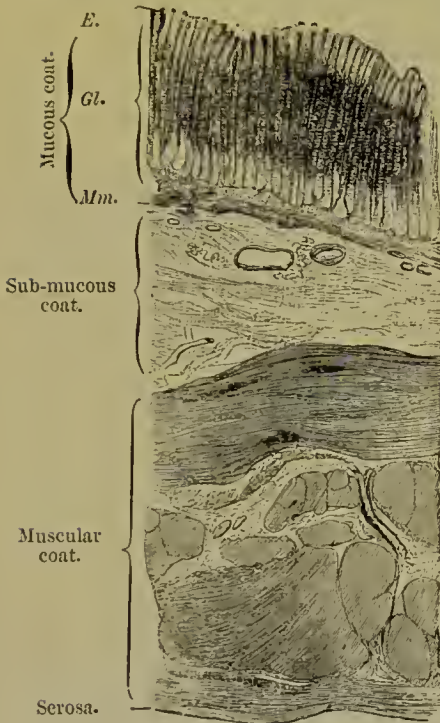


Fig. 208.



Fig. 209.



Fig. 210.

Fig. 208.—Vertical section of the wall of the human stomach $\times 15$. *E.*, epithelium; *Gl.*, glands; *Mm.*, muscularis mucosae. Fig. 209.—Goblet-cells of the stomach. Fig. 210.—Surface section of the dog's gastric mucous membrane, showing pits, *i*, *i*; *a*, the elevations round *i*, *i*.

[**Saline Cathartics.**—A salt exerts a genuine excito-secretory action on the glands of the intestines, whilst at the same time, in virtue of its low diffusibility, it impedes absorption. Thus, between stimulated secretion and impeded absorption there is an accumulation of fluid within the canal, which reaches the rectum and results in purgation. Purgation does not ensue when water is withheld from the diet for one or two days previous to the administration of the salt in a concentrated form. When a concentrated solution of a salt is administered to an animal whose alimentary canal is empty, but whose blood is in a natural state of dilution, the blood becomes rapidly very concentrated, and reaches the maximum of its concentration in from half an hour to an hour and a half; within four hours the blood has gradually returned to its normal state of concentration, without having reabsorbed fluid from the intestine. It apparently recoups itself from the tissue-fluids. The salt—sulphate of magnesia or sulphate of soda—becomes split up in the small intestine, and the acid is more rapidly absorbed than the base. A portion of the absorbed acid shortly afterwards returns to the intestines, evidently through the intestinal glands. The salt does not purge when injected into the blood, and excites no intestinal secretion; nor does it purge when injected subcutaneously, unless on account of its causing local irritation of the abdominal subcutaneous tissue, which acts reflexly on the intestines, dilating their blood-vessels, and perhaps stimulating their muscular movements (*M. Hay*).]

162. STRUCTURE OF THE STOMACH.—[The stomach receives the bolus, and secretes a juice which acts on certain constituents of the food, while by its

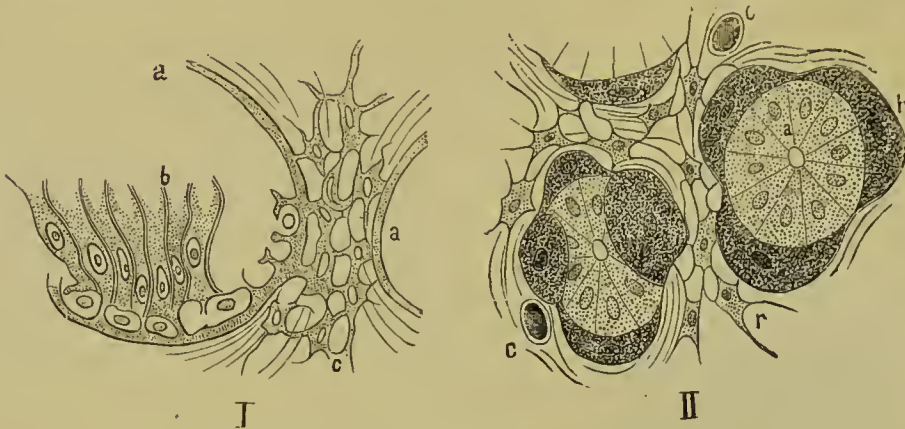


Fig. 211.

I. Transverse section of a duct of a fundus-gland—*a*, membrana propria; *b*, mucus-secreting goblet-cells; *c*, adenoid interstitial substance. II. Transverse section of a fundus-gland—*a*, chief, *h*, parietal cells; *r*, adenoid tissue; *c*, capillaries.

muscular walls it moves the latter within its own cavity, and after a time expels the partially digested products or chyme—towards the duodenum. In the adult when moderately distended its length is about 28 cm. and its greatest width 10 cm.]

[**Structure.**—The walls of the stomach consist of **four coats**, which are from without inwards (fig. 208).

- (1) The **serous layer**, from the peritoneum.
- (2) The **muscular layer**, composed of three layers of non-striped muscular fibres—(*a*) longitudinal, (*b*) circular, (*c*) oblique.
- (3) The **sub-mucous layer** of loose connective-tissue, with the larger blood-vessels, lymphatics, and nerves.
- (4) The **mucous layer**, containing the secretory glands.

The well-developed **mucous membrane** of the stomach is thrown into a series of folds or **rugæ**, in a contracted condition of the organ. With the aid of a hand-lens, it is seen to be beset with small irregular depressions or **pits** (fig. 210). Throughout its entire extent it is covered by a single layer of moderately tall, narrow, **cylindrical epithelium**, which seems to consist of **mucus-secreting goblet-cells** (fig. 209). The epithelium is sharply defined at the cardia from the stratified epithelium of the œsophagus, and also at the pylorus, from the true cylindrical epithelium with the striated disc in the duodenum. [The cells contain a plexus of fibrils, and in the passive condition seem to consist of two zones, an inner clear part, next the lumen of the organ, consisting of a substance (mucigen) which yields mucus, the attached end of the cell being granular.] The oval nucleus lies about the centre of the cells. Spindle-shaped, nucleated cells, probably for replacing the others, are said by Ebstein to occur at their bases. All the cells are open at their free ends, so that the mucus

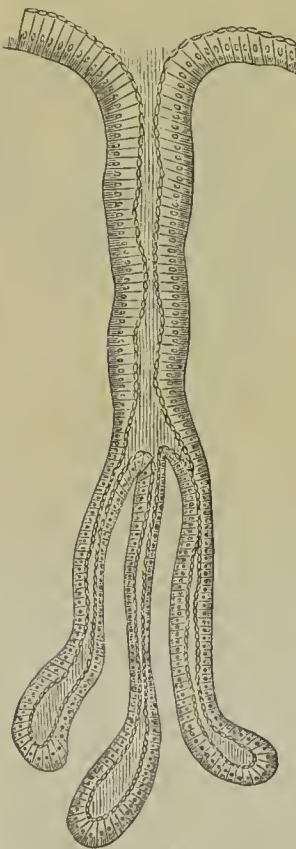


Fig. 212.

Isolated pyloric gland.

occur at their bases. All the cells are open at their free ends, so that the mucus

is readily discharged, leaving the cells empty. Numerous **tubular glands** of *two* distinct kinds are placed vertically, like rows of test-tubes, in the mucous membrane.

The **cardiac portion** of the gastric mucous membrane consists of a number of microscopic tubular glands [5 mm. to 2 mm. in length and 50–80 μ in width], placed side by side in a vertical position,—the **fundus-glands** of Heidenhain, otherwise called peptic, or cardiac. Several gland-tubes, which are wider below, usually open into the duct (fig. 213). Each gland consists of a structureless

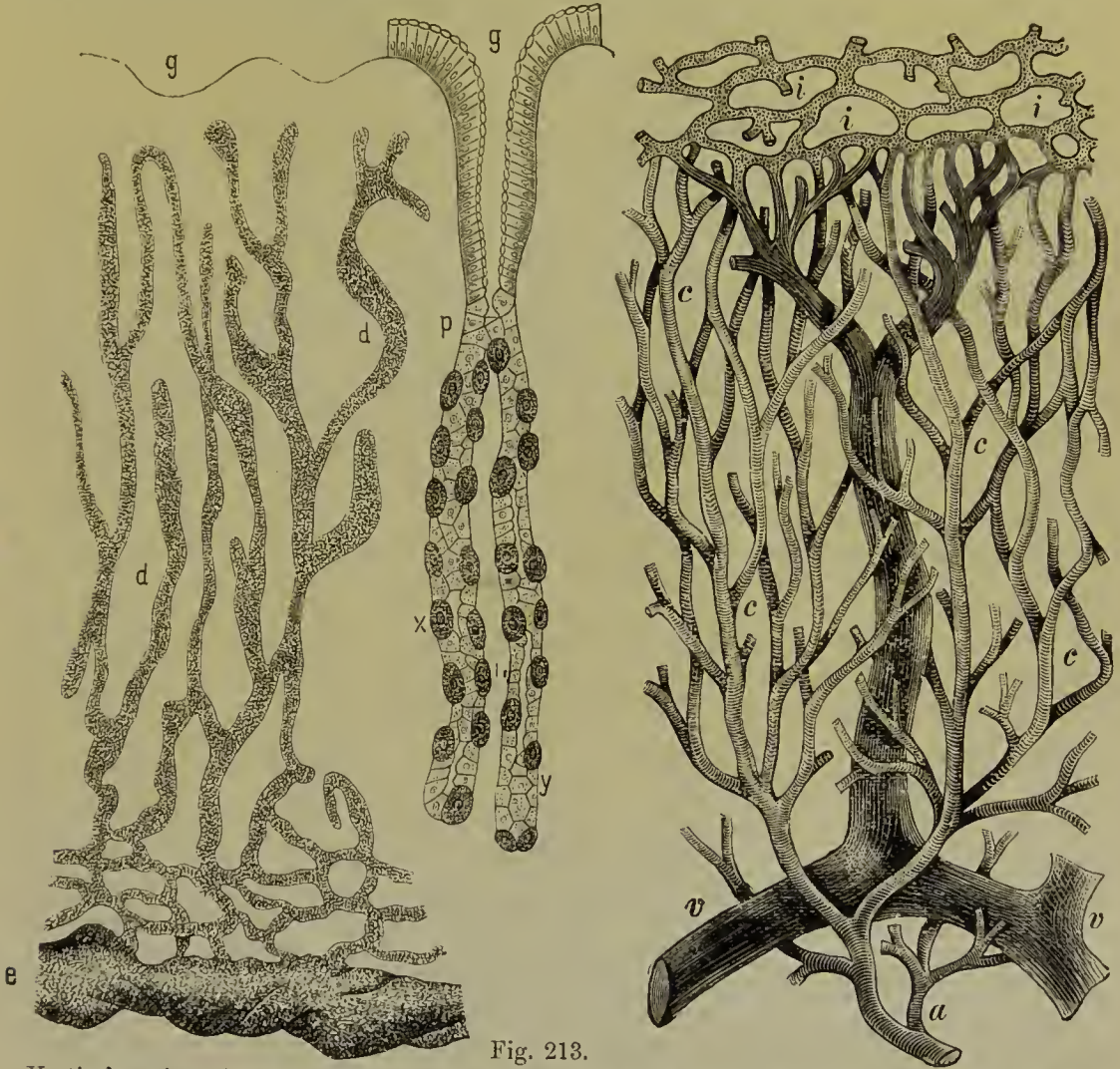


Fig. 213.

Vertical section of the gastric mucous membrane. *g, g*, pits on the surface; *p*, neck of a fundus-gland opening into a duct, *g*; *x*, parietal, and *y*, chief cells; *a*, *v*, *c*, artery, vein, capillaries; *d*, *d*, lymphatics, emptying into a large trunk, *c*.

membrana propria with anastomosing branched cells in relation with it. [Each gland has a "mouth," by which it opens into the stomach; the mouth and duct together form about one-third of the gland. The deeper part of the gland, called the "body" or "secretory part," the largest part of the gland, is joined to the duct by a "neck."] The **duct** is short, about one-fifth to one-third of the whole tube, and is lined by a layer of cells like those lining the stomach, while the **secretory part** of the tubes is lined throughout by a layer of faintly granular, short, small, polyhedral, or columnar nucleated cells. These cells border the very narrow tortuous lumen, and are called **principal, chief, central** (fig. 211, II, *a*), or **adelomorphous cells**

(ἀδελος, hidden). At various places, between these cells and the membrana propria, are large, oval, or angular, well-defined, coarsely granular, densely reticulated, nucleated cells, the **parietal** cells of Heidenhain, the **delomorphous** cells of Rollett, the **oxyntic** (ὀξύναι, to sharpen, acidulate), or acid-forming cells of Langley (fig. 211), (II, *h*), or **ovoid** cells. They are most numerous in the neck of the glands, and less so and larger in the deep blind end or fundus of the tubes. These cells do not form a continuous layer, and are stained deeply by osmic acid and aniline blue (fig. 217), so that they are readily distinguished from the other cells. They bulge out the membrana propria of the gland opposite where they are placed. The parietal cells in man are said to reach to the lumen of the gland-tubes (*Stöhr*). Isolated cells are sometimes found under the epithelium of the surface of the stomach, and occasionally in individual pyloric glands. The fundus-glands are most numerous (about five millions), and are of considerable size in the fundus. At the cardia there is a circular layer of gland-tubes without parietal cells which secrete a diastatic ferment (*Edelmann*).

2. The **pyloric glands** occur only in the region of the pylorus, where the mucous membrane is more yellowish-white in colour (fig. 212). These glands are generally branched at their lower ends, so that several tubes open into a single duct [which, in contra-distinction to the duct of the cardiac glands, is wide and long, extending often to half the depth of the mucous membrane. They are not so closely packed as the fundus glands. The mouth and **duct** are lined by epithelium like that lining the stomach, while the **secretory part** is lined by a single layer of short, finely granular, columnar cells, whose secretion is quite different from that of the cells lining the duct. The lumen is well defined. Nussbaum has occasionally found other cells, which stain deeply with osmic acid, between the bases of these. The appearance of the cells differs according to their state of physiological activity (figs. 215, 216). When they are exhausted they are smaller and more granular, owing to the denser reticulation of their network; at any rate they are granular in preparations hardened in alcohol (fig. 216). There are no parietal cells.] [Mahl by tryptic digestion has shown that the basement membranes of the gastric and other intestinal glands can be resolved into fibrils.]

3. The glands are supported by very delicate connective-tissue mixed with adenoid tissue (fig. 211). Below this are two layers, circular and longitudinal, of non-striped muscle, the **muscularis mucosæ** (fig. 208, *Mm.*), and from it fine processes of smooth muscular fibres pass up between groups of the glands towards the free epithelial surface of the mucous membrane. Perhaps these processes are concerned in emptying the glands. [In the gastric mucous membrane of the cat, there is a clear homogeneous layer, which is stained red by picro-carmin, and placed immediately internal to the muscularis mucosæ. It is pierced by the processes passing from the muscularis mucosæ.]

Masses of **adenoid tissue** occur in the mucous membrane, especially near the pylorus, constituting **lymph-follicles**, which are comparable to the solitary glands of the small intestine. The **lymphatics** are numerous, and begin close under the epithelium by dilated extremities or loops (fig. 213, *d*); they run vertically between the gland-tubes and anastomose in the mucosa between the gland-tubes, which they envelop in sinus-like spaces. They join large trunks in the mucosa; another plexus of large vessels exists in the sub-mucosa (*Lovén*).

[**The Nerves.**—A plexus of non-medullated nerve-fibres and a few ganglion cells exist in the muscular coat [*Auerbach's*], and another [*Meissner's*] in the sub-mucosa.]

The **blood-vessels** are very numerous (fig. 214). Small arterial branches, *a*, run in the sub-mucosa, and ascend between the glands to form a longitudinal capillary network, *c, c*, under the epithelium, and between its meshes the gland-

ducts open, *g*. The veins gradually collect from this horizontal capillary network, and run towards the large veins of the sub-mucosa, *v*.

[**Transition from stomach to duodenum.**—If a section be made through the junction of the stomach with the duodenum, it shows the appearances presented in fig. 214. The glands of Brunner in the duodenum are seen to be homologous

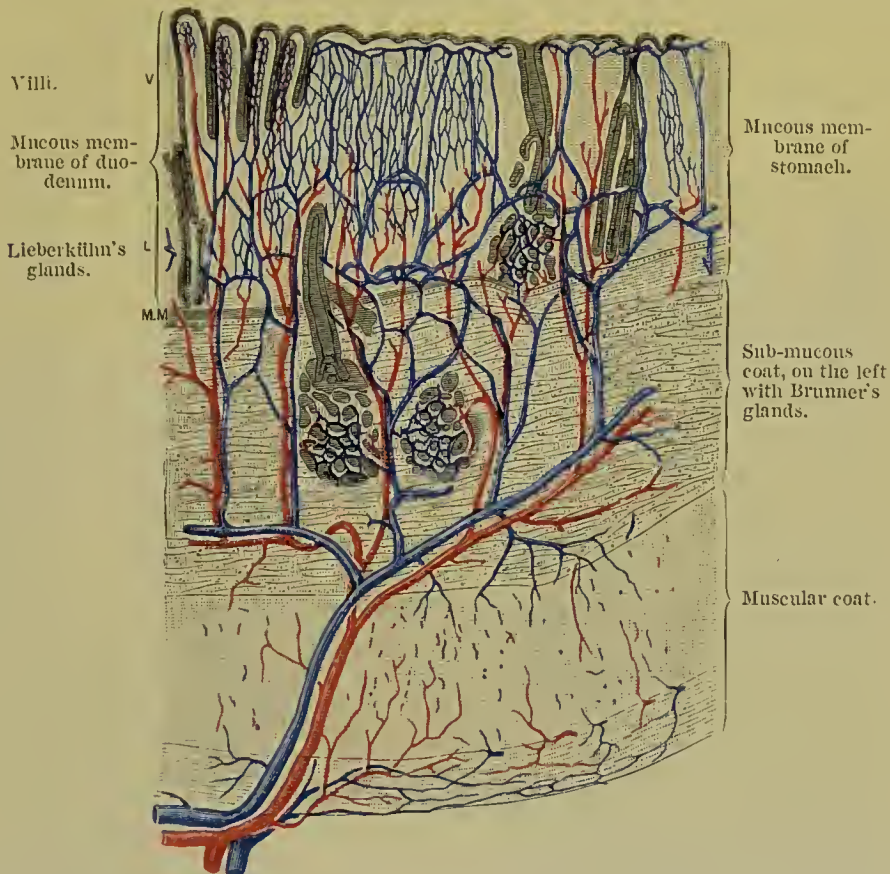


Fig. 214.

Vertical section of the junction between the stomach and duodenum. The blood-vessels injected. V, villi; MM, muscularis mucosae; arteries red, veins blue.

with the pyloric glands, but in the duodenum the acini of the glands of Brunner lie in the sub-mucous coat, while in the mucous coat itself the glands of Lieberkühn appear, and with them the villi so characteristic of the small intestine.]

163. THE GASTRIC JUICE.—**Properties.**—The gastric juice is a tolerably clear colourless fluid, with a strong acid reaction, sour taste, and peculiar characteristic odour; it rotates the plane of polarised light to the left. It is not rendered turbid by boiling, and resists putrefaction for a long time. Its specific gravity = 1002.5 (dog, 1005), and it contains only $\frac{1}{2}$ per cent. of solid constituents. The quantity secreted in 24 hours was estimated by Beaumont, from observations upon Alexis St Martin, who had a gastric fistula (1834)—at only 180 grms. daily (!); by Grunewald (1853), in a similar case, as equal to 26.4 per cent. of the body-weight; while Bidder and Schmidt (from corresponding observations on dogs) estimated it as equal to $6\frac{1}{2}$ kilos. daily, corresponding to $\frac{1}{10}$ of the body-weight. It contains:—

(1) **Pepsin**, the characteristic hydrolytic ferment or enzyme, which in an

acid medium dissolves proteids. E. Schütz obtained 0.41 to 1.17 per cent. from a fasting person by means of the œsophageal sound.

(2) **Free hydrochloric acid** (*Prout*, 1824), 0.2 to 0.3 (*Richet*, 0.8 to 2.1) per cent.; (in the dog, 0.52 per cent.). The acid occurs as *free hydrochloric acid*, as from the gastric juice there can always be obtained more free chlorine than bases to which the latter can be united (*C. Schmidt*). Lactic acid is usually met with, but it arises from the fermentation of the carbohydrates of the food.

Tests.—Free hydrochloric acid is detected by the following reactions:—0.025 per cent. solution of methyl-violet becomes blue, especially after tannic acid has been added to the fluid; or

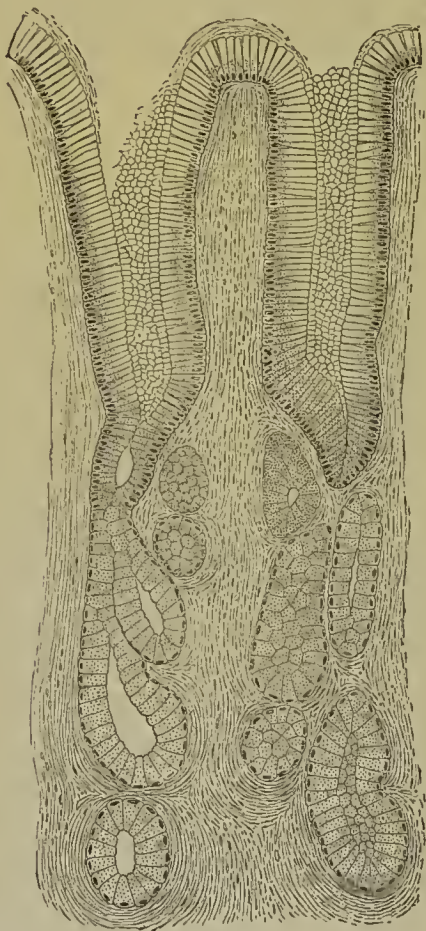


Fig. 215.

Section of the pyloric mucous membrane.

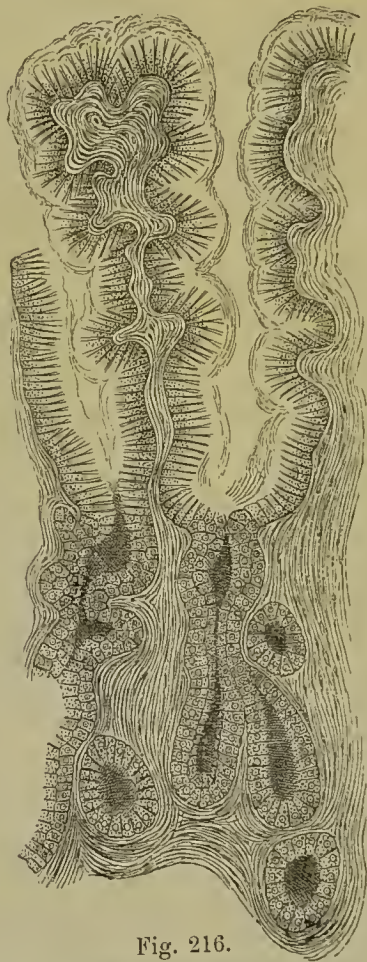


Fig. 216.

Pyloric glands, showing changes of the cells during digestion.

alkaline solution of *oo-tropæolin* becomes lilac; or, red Bordeaux wine, treated with amylie alcohol until its colour *almost* disappears, becomes rose-coloured. An amylie alcohol extract of ripe bilberries is made red by dilute HCl. [Günzburg recommends an alcoholic solution of *phloroglucin-vanillin*. 2 grams of phloroglucin are mixed with 1 gram of vanillin in 30 grams of absolute alcohol, which gives a yellowish-red solution. Concentrated and even very weak mineral acids cause, with this solution, a bright red colour with the formation of bright red crystals, while concentrated organic acids do not affect it. For gastric juice, mix equal quantities of the filtered gastric juice and the above solution in a watch-glass, and evaporate carefully, not allowing it to boil; a red pellicle with red crystals indicates the presence of minute traces of hydrochloric acid. **Congo-red**, either in solution or as congo-red papers, becomes blue, but the reaction is interfered with by the presence of ammonia, or ammoniacal salts.]

Lactic Acid.—The freshly-prepared blue solution of 10 c.c. of a 4 per cent. solution of carbolic acid, with 20 c.c. of distilled water, and 1 drop of liquor ferri perchloride, is changed to

yellow by lactic acid (*Uffelmann*). Allow the fluid to drop into the test; at the point of contact there is a citron-yellow colour.

(3) The large amount of **mucus** covering the surface of the mucous membrane is secreted by the goblet-cells of the mucous membrane (§ 162).

(4) **Mineral salts** (2 per 1000).

They are chiefly sodium and potassium chlorides, less calcic chloride (ammonium chloride, also in animals), and the compounds of phosphoric acid with lime, magnesium, and iron.

(5) **A milk-curdling ferment** (rennet or rennin).

Amongst foreign substances, which may be introduced into the body, the following appear in the gastric juice—**HI**, after the use of potassium iodide—potassium sulphocyanide, ferric lactate, and sugar; and ammonium carbonate in uræmia.

[Composition of Gastric Juice (*Hoppe-Seyler* after *C. Schmidt*).

Constituents.	I. Human.	II. Dog.		IV. Sheep.
		With saliva.	No saliva.	
Water, ...	994.404	971.171	973.062	986.143
Organic matter, ...	3.195	17.336	17.127	4.055
Free HCl, ...	0.200	2.337	3.050	1.234
CaCl ₂ , ...	0.061	1.661	0.624	0.114
NaCl, ...	1.465	3.147	2.507	4.369
KCl, ...	0.550	1.073	1.125	1.518
NH ₄ Cl, ...	...	0.537	0.468	0.473
Ca ₃ 2(PO ₄), ...	0.125	2.294	1.729	1.182
Mg ₃ 2(PO ₄), ...		0.323	0.226	0.577
FePO ₄ , ...		0.121	0.082	0.331

Good human saliva is not so dilute or so poor in HCl as No. I. Szabo has found even 3 of HCl per 1000 in man.]

[**Comparative.**—The above table shows that the gastric juice of mammals has approximately the same composition as that of man, but there is more acid in the case of the carnivora than in herbivora and man. The acidity is very considerable in fishes. It is said that in certain invertebrates (crustaceans), the gastric juice is alkaline.]

[The pepsin in frogs seems to be different from that in mammals, at least it is active at 0° C. at which temperature mammalian pepsin is inactive.]

[The gastric juice of new-born dogs and rabbits does not contain pepsin, but it appears a few days after birth. In the dog, according to Hammarsten, pepsin is formed until the third week after birth; while pepsin is present in the human foetal mucous membrane just before birth, the acid appears much sooner.]

164. SECRETION OF GASTRIC JUICE.—After the discovery of the two kinds of glands in the stomach and the two kinds of cells in the fundus-glands, the question arose as to whether the different constituents of gastric juice were formed by different histological elements.

Changes of the Cells during Digestion.—During the course of digestion, the cells of the fundus (and pyloric glands, dog) undergo important changes (*Heidenhain*). During hunger, the chief cells are *clear* and large, the parietal investing cells are small, the pyloric cells *clear* and of moderate size. During the first six hours of digestion, the chief cells become *enlarged* and moderately turbid or granular, the parietal cells also *enlarge*, while the pyloric cells remain unchanged (fig. 217). The chief cells become *diminished* and more turbid or granular until the ninth hour, the parietal cells are still swollen, and the pyloric cells enlarge (fig. 217, D). During the last hours of digestion, the chief cells again become larger and clearer, the parietal cells diminish, the pyloric cells decrease in size and become turbid (figs. 215, 216).

[Langley gives a different description of the appearances presented by these cells. The results may be reconciled by remembering that the gland-cells were examined under different conditions. The secretory cells consist of a cell-substance composed of (a) a framework of living protoplasm, either in the form of an intracellular fibrillar network, or in flattened bands. The meshes of this framework enclose at least two chemical substances, viz., (b) a hyaline substance in contact with the framework, and (c) spherical granules which are embedded in the hyaline substance. During active secretion, the granules decrease in number and size, the hyaline substance increases in amount, the network grows. This is the reverse of what is stated above as

the observation of Heidenhain, but the granular appearance described by Heidenhain after secretion is very probably due to the action of the hardening agent, alcohol. Langley found that in the living condition, or after the use of osmic acid, in some animals at least, the chief cells are granular during rest, but during a state of activity two zones are differentiated—an outer one, which is clear, owing to the disappearance of the granules, and an inner more or less granular one. Granules reappear in the outer part after rest. During digestion, the parietal cells increase in size, but do not become granular. In all cells containing much pepsinogen distinct granules are present, and the quantity of pepsinogen varies directly with the number and size of the granules. In the glands of some animals there is little difference between the resting and active phases. Compare *Serous Glands*, § 143, and *Pancreas*, § 168.]

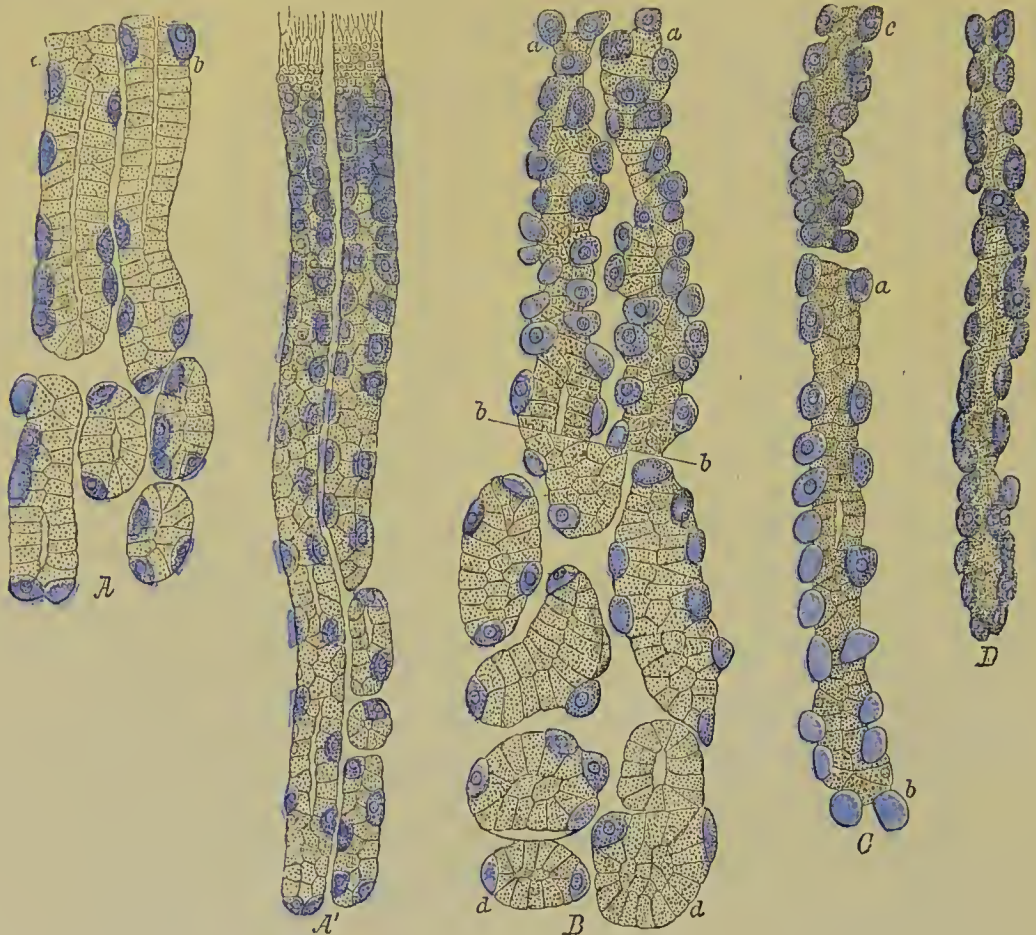


Fig. 217.

Fundus glands of dog stained with aniline blue. A and A', when animal was starved; B, first stage of digestion, enlargement of the chief cells; C and D, second stage of digestion, progressive diminution and increased turbidity of the chief cells (*Heidenhain*).

Pepsin is formed in the **chief cells** of the fundus-glands. When these are large, they contain much pepsin; when they are turbid, the amount is small. The pyloric glands are also said to secrete pepsin, but only to a small extent. Pepsin accumulates during the first stage of hunger, and it is eliminated during digestion, and also during prolonged hunger. Pepsin, *as such*, is not present within the cells, but only as a "mother-substance," a **pepsinogen-substance (zymogen)**, or **pro-pepsin**, which occurs in the granules of the chief cells. This zymogen, or mother-substance, by itself, has no effect upon proteids; but if it be treated with hydrochloric acid or sodium chloride, it is changed into pepsin. Pepsin and

pepsinogen may be extracted from the gastric mucous membrane by means of water free from acids.

[The chief reasons adduced for the view that the chief cells secrete pepsin are as follows :—(1) The principal cells disappear by auto-digestion when the mucous membrane is placed in 1 per cent. hydrochloric acid, while the parietal cells swell up and do not disappear ; (2) There is a relation between the volume of these cells and the quantity of pepsin obtainable from the mucous membrane ; (3) The pyloric region, which contains no parietal cells, also secretes pepsin ; (4) In frogs the pepsin is formed in the œsophageal glands, which contain only cells analogous to the principal cells, while the stomach contains glands with parietal cells, but it secretes acid, and no pepsin ; (5) In the bat during hybernation the principal cells disappear almost entirely while digestive activity is suspended.]

[**Pepsinogen and Pepsin.**—Glycerin extracts very little pepsin from the perfectly fresh gastric mucous membrane, but a large amount is afterwards obtained by extracting it with dilute hydrochloric acid, or with this acid and glycerin. The relative amount of pepsinogen and pepsin in a fluid may be determined approximately by the method of Langley and Edkins. A 1 per cent. solution of sodic carbonate exerts a greater destructive action on pepsin than on pepsinogen, while a current of CO_2 destroys pepsinogen to a greater extent than pepsin. Both substances are unaffected by CO_2 , but are destroyed at 54° to 57°C.]

[That pepsinogen exists in the mucous membrane is proved as follows :—Extract the mucous membrane with water, or glycerin free from acid, until no more pepsin is obtainable from the membrane. Then treat the latter with dilute hydrochloric acid or sodic chloride, when a fresh quantity of pepsin is at once obtainable. More pepsin is formed or set free by the action of these re-agents upon some other body, which has been called propepsin and pepsinogen.]

The pyloric glands also secrete pepsin but no acid. Klemensiewicz excised in a living dog the pyloric portion of the stomach, and afterwards stitched together the duodenum, and the remaining part of the stomach. The excised pyloric part, with its vessels intact, he stitched to the abdominal wall, after sewing up its lower end. The animals experimented on died, at the latest, after six days. The secretion of this part was thin, *alkaline*, and contained 2 per cent. of solids, including **pepsin**.

[**Pyloric Fistula.**—In fig. 218, P represents the excised pyloric portion, C the cardiac. The parts *a*, *a*, and *a'* *a'* were then stitched together, and the continuity of the organ established. The lower end (*d*) of P was closed by sutures, while the edges of P at *o* were stitched to the abdominal walls, thus making a pyloric fistula.]

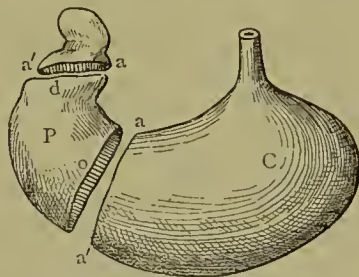


Fig. 218.

Diagram of Klemensiewicz's experiment (*Stirling*).

In the **frog** the alkaline glands of the œsophagus contain only chief cells which produce pepsin ; while the stomach has glands which secrete acid (and perhaps some pepsin), and are lined by parietal cells.

Amongst **fishes** the carps have no fundus-glands in the stomach (*Luchan*). [The secreting portions of glands of the cardiac sac (crop) of the herring are lined by a *single* layer of polygonal cells (*W. Stirling*).]

The **hydrochloric acid is formed**, according to Heidenhain, by the **parietal cells**. It occurs on the free surface of the gastric mucous membrane as well as in the ducts of the fundus-glands. The deep parts of the glands are usually alkaline. Free HCl is detected in human gastric juice, within 45 minutes to 1 or 2 hours after a moderate meal, but in 10 to 15 minutes in a fasting condition after drinking water ; the amount gradually increases during the process of digestion. Lactic acid, perhaps derived from the food, is found in the stomach immediately after taking food, after half an hour, along with HCl , while after an hour only HCl is found (*Ewald and Boas*).

Cl. Bernard injected lactate of iron, and some time afterwards potassium ferrocyanide, into the veins of a dog. After death, blue coloration occurred only in the *upper acid* layers of the mucous membrane. Nevertheless, we must assume that the hydrochloric acid is secreted in the parietal cells of the fundus of the glands, and that it is rapidly carried to the surface along with the pepsin. Brücke neutralised the surface of the gastric mucous membrane with

magnesia usta, chopped up the mucous membrane with water, and left it for some time, when the fluid had again an acid reaction.

As to the **formation of a free acid**, the following statements may be noted:—The parietal cells form the hydrochloric acid from the chlorides which the mucous membrane takes up from the blood. According to Voit, the formation of acid ceases, if chlorides be withheld from the food. Maly suggests that the active agent is lactic acid, which splits up sodium chloride and forms free HCl. The base set free is excreted by the urine, rendering it at the same time less acid. The formation of acid is arrested during hunger. According to H. Schultz, watery solutions of alkaline and earthy chlorides are decomposed, even at a low temperature, by CO_2 , free hydrochloric acid being formed.

[If thin sections of the fresh mucous membrane be placed for a day in lactate of iron, and then treated with potassic ferrocyanide, Schrwald finds that the parietal cells become dark blue, while the chief cells remain colourless, so that the chief cells appear to be alkaline and the parietal cells acid.]

[The **source of the HCl** is undoubtedly the **sodic chloride** in the blood and lymph, but what other acid displaces the HCl is a matter of conjecture. In this connection, it is important to remember that Jul. Thomsen has shown that every acid can displace a part of another acid from its combination with its base, and the weaker acid may even combine with the greater part of the base. Thomsen calls this "**avidity**." Even strong mineral acids may be displaced by weak organic ones. Thus the free CO_2 in the alkaline blood may set free a small quantity of HCl from the sodic chloride. What is still more remarkable is, that the free HCl should be transferred by the cells towards the gland-duct while the sodic carbonate diffuses towards the blood and lymph.]

[The **milk-curdling ferment** or **rennin** exists in the mucous membrane in the state of a zymogen, from which it is formed under the action of acids. According to Langley it exists in the principal cells.]

Secretion.—[The secretion of gastric juice is intermittent except in the case of those animals like the rabbit, whose stomachs always contain food.] When the stomach is **empty**, there is usually no secretion of gastric juice; this takes place only after appropriate (mechanical, thermal, or chemical) stimulation. In the normal condition, it takes place immediately on the introduction of food, but also of indigestible substances, such as pebbles. The mucous membrane becomes red, and the circulation more active, so that the venous blood becomes brighter. [That the vagi are concerned in this vascular dilatation is proved by the fact that if both nerves be divided during digestion, the gastric mucous membrane becomes pale (*Rutherford*).] The secretion is probably caused reflexly, and the centre perhaps lies in the wall of the stomach itself (Meissner's plexus in the sub-mucous coat). It is asserted that the idea of food, especially during hunger, excites secretion. As yet we do not know the effect produced upon the secretion by stimulation or destruction of other nerves, *e.g.*, vagus, sympathetic. [There is no nerve passing to the stomach, whose stimulation causes a secretion of gastric juice, as the chorda tympani does in the submaxillary gland. If the vagi be divided sufficiently low down not to interfere with respiration, the introduction of food still causes a secretion of gastric juice; even if the sympathetic branches be divided at the same time, secretion still goes on (*Heidenhain*). Division of the vagi in the neck is not a satisfactory experiment in relation to the secretion of gastric juice, for this experiment produces so many other effects. If the vagi be divided below the origin of the pulmonary and cardiac branches, gastric juice containing pepsin and capable of digestion is said by some observers to be still secreted (see under). This experiment points to the existence of local secretory centres in the stomach. But there is evidence to show that there is some connection, perhaps indirect, between the central nervous system and the gastric glands. Richet observed a case of complete occlusion of the œsophagus in a woman, produced by swallowing a caustic alkali. A gastric fistula was made, through which the person could be nourished. On placing sugar or lemon juice in the person's mouth, Richet

observed a secretion of gastric juice. In this case no saliva could be swallowed to excite secretion, so that it must have taken place through some nervous channels. Even the sight or smell of food caused secretion. Emotional states also are known to interfere with gastric digestion.]

[In dogs Pawlow made a gastric fistula, divided the œsophagus, and stitched the two cut ends of the latter into the wound in the neck. After recovery of the animals he found that flesh, when eaten, excited a copious reflex secretion of gastric juice (20 c.c. in 5 minutes) in an empty stomach. Of course the food in this case escaped by the divided œsophagus and did not enter the stomach. This effect was not altered by section of the splanchnic nerves. Division of the vagi, however, completely abolished the reflex. After section of the vagi, for several days only strongly acid mucus flowed from the stomach, but it had scarcely any action on proteids. Stimulation of the peripheral end of the divided left vagus caused a clear watery fluid to flow from the fistula, which, although less acid than normal juice, was capable of digesting proteids.]

Effect of Absorption of peptic products.—Heidenhain isolated a part of the mucous membrane of the *fundus* so as to form a blind sac of it, and he found that mechanical stimulation caused merely a scanty *local* secretion at the spots irritated. If, however, at the same time, absorption of digested matter also occurred, secretion took place over larger surfaces. [He distinguishes a primary and merely local secretion excited by the mechanical stimulus of the ingesta, and a secondary depending on absorption, and extending to the whole of the mucous membrane.]

The statement of Schiff, that active gastric juice is secreted only after absorption of the so-called **peptogenic substances** (especially dextrin) is contradicted by other observers.

The **acid contents of the stomach** called **chyme**, which pass into the duodenum after gastric digestion is completed, are *neutralised* by the alkali of the intestinal mucous membrane and the pancreatic juice, [at the same time a precipitate is formed and deposited on the walls of the duodenum, and it carries the pepsin down with it]. Part of the pepsin is reabsorbed as such, and is found in traces in the urine and muscle juice (*Brücke*). If the gastric juice be completely discharged externally through a gastric fistula, the alkalinity of the intestine is so strong that the urine becomes alkaline (*Maly*).

The acid gastric juice of the **new-born child** is already fairly active; casein is most easily digested by it, then fibrin and the other proteids (*Zweifel*). When the amount of acid is too great in the stomach of sucklings, large firm indigestible masses of casein are apt to be formed, especially after the use of cow's milk (§ 230).

[Action of Drugs on Gastric Secretion.]—Dilute alkalies, if given before food; saliva; some substances called **peptogens** by Schiff, such as dextrin and peptones, alcohol and ether, all excite secretion, the last being very powerful. When the secretion is excessively acid, *antacids* are given, some diminishing the acidity in the stomach, as the carbonates and bicarbonates of the alkalies, liquor potassæ, and the carbonate of magnesia; while the citrates and tartrates of the alkalies, becoming converted into carbonates in their passage through the organism, diminish the acidity of the urine.] Small doses of **alcohol**, introduced into the stomach, increase the secretion of gastric juice; large doses arrest it. Artificial digestion is affected by 10 per cent. of alcohol, is retarded by 20 per cent., and is arrested by stronger doses. Beer and wine hinder digestion, and in an undiluted form interfere with artificial digestion.

165. METHODS OF OBTAINING GASTRIC JUICE.—**Historical.**—Spallanzani caused starving animals to swallow small pieces of sponge enclosed in perforated lead capsules, and after a time, when the sponges had become saturated with gastric juice, he removed them from the stomach. To avoid the admixture of saliva, the sponges are best introduced through an opening in the œsophagus. Dr Beaumont (1825), an American physician, was the first to obtain human gastric juice, from a Canadian named Alexis St Martin, who was injured by a gun-shot wound, whereby a permanent gastric fistula was established. Various substances were introduced through the external opening, which was partially covered with a fold of skin, and the time required for their solution was noted. Bassow (1842), Blondlot (1843), and Bardeleben (1849) were thereby led to make artificial gastric fistulæ.

Gastric Fistula.—The anterior abdominal wall is opened by a median incision just below the ensiform cartilage, the stomach is exposed, and its anterior wall opened and afterwards stitched to the margins of the abdominal walls. A strong cannula is placed in the fistula thus formed. The tube is kept corked. If the ducts of the salivary glands be tied, a perfectly uncomplicated object for investigation is obtained.

According to Leube, dilute human gastric juice may be obtained by means of a syphon-like tube introduced into the stomach. Water is introduced first, and after a time it is withdrawn.

An important advance was made when Eberle (1834) prepared **artificial gastric juice**, by extracting the pepsin from the gastric mucous membrane with dilute hydrochloric acid. Four litres of solution of hydrochloric acid, containing 4 to 8 c.c. HCl per 1000, are sufficient to extract the chopped-up mucous membrane of a pig's stomach. Half a litre is infused with the stomach and renewed every six hours. The collected fluid is afterwards filtered. The substance to be digested is placed in this fluid, and the whole is kept at the temperature of the body, but it is necessary to add a little HCl from time to time (*Schwann*). The HCl may be replaced by ten times its volume of lactic acid and also by nitric acid; while oxalic, sulphuric, phosphoric, acetic, formic, succinic, tartaric, and citric acids are much less active; butyric and salicylic acids are inactive.

Von Wittich's Method.—(a) Glycerin extracts pepsin in a very pure form. The mucous membrane is rubbed up with powdered glass until it forms a pulp, mixed with glycerin, and allowed to stand for eight days. The fluid is pressed through cloth, and the filtrate mixed with alcohol, thus precipitating the pepsin, which is washed with alcohol and afterwards dissolved in the dilute HCl, to form an artificial digestive fluid. (b) Or the mucous membrane may be placed for twenty-four hours in alcohol, and afterwards dried and extracted for eight days with glycerin. (c) Wm. Roberts has used other agents for extracting enzymes (§ 148).

Preparation of Pure Pepsin.—Brücke pours on the pounded mucous membrane of the pig's stomach a 5 per cent. solution of phosphoric acid, and afterwards adds lime-water until the acid reaction is scarcely distinguishable. A copious precipitate, which carries the pepsin with it, is produced. This precipitate is collected on cloth, repeatedly washed with water, and afterwards dissolved in very dilute HCl. A copious precipitation is caused in this fluid by gradually adding to it a mixture of cholesterol in four parts of alcohol and one of ether. The cholesterol pulp is collected on a filter, washed with water containing acetic acid, and afterwards with pure water. The cholesterol pulp is placed in ether to dissolve the cholesterol, and the ether is then removed. The small watery deposit contains the pepsin in solution.

Pepsin so prepared is a colloid substance; it does not react like albumin with the following tests, viz.:—It does not give the xanthoprotein reaction (§ 248), is not precipitated by acetic acid and potassium ferrocyanide, nor by tannic acid, mercuric chloride, silver nitrate, or iodine. In other respects it belongs to the group of albuminoids. It is rendered inactive in an acid fluid by heating it to 55° to 60° C.

166. PROCESS OF GASTRIC DIGESTION.—[In the process of gastric digestion we have to consider—

1. The secretion of gastric juice and its action on food.
2. The absorption of the products of this digestion.
3. The movements of the stomach itself.]

Chyme.—The finely divided mixture of food and gastric juice is called *chyme*. The gastric juice acts upon certain constituents of chyme.

I. Action on Proteids.—Pepsin and the dilute hydrochloric acid, at the temperature of the body, transform proteids into a *soluble* and *diffusible* form, to which Lehmann (1850) gave the name of "**peptone**" (§ 249, III.). Fibrin (or coagulated proteids) first becomes clear and swollen up. [There seems to be a close relation between the acid and the ferment, so much so that some have spoken of it as "pepsin-acid" and others as "pepto-hydrochloric acid."]

[It is commonly stated that the first product formed during the gastric digestion of proteids is **syntonin** or **para-peptone**, then **hemi-albumose** or **pro-peptone**, and finally **peptone**. The products vary, however, with the proteid digested. Kühne has shown that the proteid molecule is split up, and yields two groups, which he calls **hemi-peptone** and **anti-peptone** (p. 296). A mixture of the two he calls **ampho-peptone**. **Hemi-peptone** can be split up into leucin and tyrosin by trypsin, while the **anti-peptone** does not undergo this change. The intermediate body, or pro-peptone, is really a mixture of several bodies. Kühne called it hemi-albumose. These intermediate bodies from albumin are called **albumoses**, from globulins **globuloses**, from casein **caseoses**. Halliburton calls all these intermediate bodies "**proteoses**."]]

Properties of Hemi-albumose. Although a composite body, hemi-albumose gives the following reactions:—It is highly soluble in water; when heated to 50° to 60° it becomes somewhat turbid, but when boiled it becomes clear, and gets turbid again on cooling. This effect is most marked when it is treated with acetic acid and sodic chloride, or the latter alone. It is precipitated by acetic acid and potassic ferrocyanide, but the precipitate disappears on heating and reappears on cooling. It gives the biuret rosy tint reaction like peptones. It is *precipitated by nitric acid*, and the precipitate adheres to the glass, but is *soluble in the acid with the aid of heat*, yielding a yellow fluid, but is *precipitated on cooling*. It is precipitated by boiling with acetic acid and a strong solution of sodic sulphate, metaphosphoric acid, and pyrogallie acid (*Kühne*). It is said to be present in all animal tissues except muscle and nerve (§ 293).

[**Albumoses** are the first products of the splitting up of proteids by enzymes, and from them peptones are ultimately formed. They may be made from Witte's peptone, or by the peptic digestion of fibrin. Such a mixture, on being neutralised with sodic carbonate, gives a copious precipitate of para-peptones, which can be filtered off, leaving a clear solution of albumoses. Para-peptones are said to be closely related to acid-albumin or syntonin. On saturating the clear fluid with NaCl, a dense white precipitate, consisting of three albumoses, called **proto-dys**, and **hetero-albumose** is obtained; a fourth, **deutero-albumose**, remains in solution, but can be precipitated by adding acetic acid. If the albumose precipitate be treated with 10 per cent. NaCl solution, proto- and hetero-albumose are dissolved, leaving dys-albumose undissolved. Dialysis of the saline solution precipitates hetero-albumose, leaving proto-albumose in solution. It is probable however, that hetero- and dys-albumose are identical, or that the former is merely an insoluble form of the latter. The albumoses are bodies intermediate between albumins and peptones, and of the three, deutero-albumose is nearest to peptones. An important character is that they do not dialyse or diffuse readily. The albumoses also are produced by the activity of many micro-organisms and doubtless play an important part in many pathological processes (§ 249).]

Properties of the Albumoses.—**Proto-albumose** is soluble in distilled water, is not changed by heat, but is precipitated by saturation of the solution with sodic chloride, by HNO_3 , acetic acid and potassic ferrocyanide, copper sulphate, mercuric chloride. **Deutero-albumose** is very like the foregoing, but it is not precipitated by HNO_3 or on adding sodic chloride to saturation, but precipitation occurs when 20 to 30 per cent. of acetic acid is added. **Hetero-albumose** resembles a globulin in its properties; it is insoluble in distilled water, but is soluble in saline solutions (10 to 15 per cent.), and is partly precipitated from its solution by saturation with NaCl or by dialysis. It is coagulated by heat. All give the rosy-pink colour with the biuret-reaction, and they are all precipitated by saturation with neutral ammonia sulphate, which peptones are not (*Kühne and Chittenden*).] See also § 249.

[**Globuloses** from the globulin of ox-serum are obtained in the same way, although the ferment has much less action on globulin than on albumin. Speaking generally, they resemble the albumoses.]

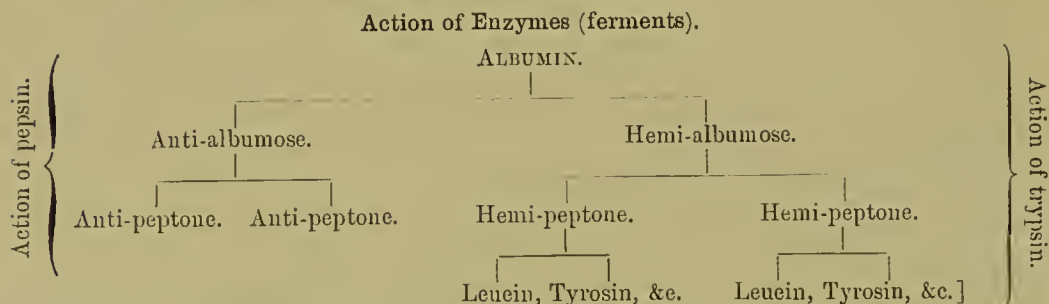
By the continued action of the gastric juice, the pro-peptone passes into a **true soluble peptone**. The unchanged albumin behaves like an anhydride with respect to the peptone. The formation of peptone is due to the taking up of a molecule of water, under the influence of the hydrolytic ferment pepsin, and the action takes place most readily at the temperature of the body. Gelatin is changed into a *gelatin-peptone*.

[**Method of separating the products of gastric digestion.** If fibrin or white of egg be digested for some time with gastric juice, these proteids will ultimately be dissolved. Neutralise the digest with sodic carbonate and a greater or less precipitate of **para-peptones** will be obtained. Filter. The filtrate contains other digested proteids. Saturate it with crystals of neutral ammonium sulphate, which will precipitate the **albumoses**; filter these off, and the solution still contains

peptone, which can be precipitated by much alcohol. Ammonium sulphate precipitates all soluble proteids except peptones.]

According to Kühne, the proteid molecule contains two preformed substances in its composition: **anti-albumin** and **hemi-albumin**. Gastric juice at first converts them into **anti-albumose** and **hemi-albumose**, and ultimately the former is converted into **anti-peptone** and the latter into **hemi-peptone** (§ 170, II.). Only the latter is capable of being split up by trypsin into leucin and tyrosin by the action of the pancreatic juice (§ 249).

[The following scheme represents the results :—



The greater the amount of pepsin (within certain limits), the more rapidly does the solution take place. The pepsin suffers scarcely any change, and if care be taken to renew the hydrochloric acid, so as to keep it at a uniform amount, the pepsin can dissolve new quantities of albumin. Still, it seems that some pepsin is used up in the process of digestion (*Grützner*). Proteids are introduced into the stomach either in a solid (coagulated) or fluid condition. Casein alone of the fluid forms is precipitated or coagulated, and afterwards dissolved. The non-coagulated proteids are transformed into syntonin, without being previously coagulated, and are then changed into pro-peptone and directly peptonised, *i.e.*, actually *dissolved*.

When albumin is digested by pepsin at the temperature of the body, a not inconsiderable amount of heat **disappears**, as can be proved by calorimetric experiment (*Maly*). Hence, the temperature of the chyme in the stomach falls 0°·2 to 0°·6 C. in two to three hours (*v. Vintschgau and Diell*).

Coagulated albumin may be regarded as the anhydride of the fluid form, and the latter again as the anhydride of peptone. The peptones, therefore, represent the highest degree of hydration of the proteids.

Hence, peptones may be formed from proteids by those reagents which usually cause hydration, *viz.*, treatment with strong acids (from fibrin, with 0·2 HCl), caustic alkalies, putrefactive and various other ferments, and ozone.

The anhydride proteid has been prepared from the hydrated form. Henniger and Hofmeister, by boiling pure peptone with dehydrating substances (anhydrous acetic acid at 80° C.), have succeeded in decomposing it into a body resembling syntonin.

Peptones.—(1) They are completely soluble in water. (2) They diffuse very easily through animal membranes. (3) They filter quite easily through the pores of animal membranes. (4) They are *not precipitated* by boiling, nitric acid, acetic acid and potassium ferrocyanide, acetic acid and saturation with common salt. (5) They are *precipitated* from neutral or feebly acid solutions by mercuric chloride, tannic acid, bile acids, and phospho-molybdic acid. (6) With Millon's reagent they react like proteids, and give a red colour, and with nitric acid give the yellow xantho-protein reaction. (7) With caustic potash or soda and a small quantity of cupric sulphate, [or Fehling's solution], they give a beautiful *rosy-red* colour, the biuret-reaction. (8) They rotate the plane of polarised light to the left.

[Kühne and Chittenden, making use of the fact that ammonium sulphate to

saturation precipitates all proteids from solution except peptone, have reinvestigated the subject, and they find that many of the peptones of commerce contain albumoses. Pure peptone has remarkable properties. When dissolved in water, it hisses and froths like phosphoric anhydride, heat is evolved, and a brown solution is formed. It is difficult to preserve it. It is not precipitated by NaCl, or NaCl and acetic acid, but is completely precipitated by phospho-tungstic and phospho-molybdic acids, tannin, iodo-mercuric iodide, picric acid. Peptones have a cheesy taste, while albumin and albumoses are tasteless.]

The biuret-reaction is obtained with hemi-albumose, as well as with a form of albumin, which is formed during artificial digestion and is soluble in alcohol. It is called "alkophyr" by Brücke. [Darby's fluid-meat gives all the above reactions, and is very useful for studying the tests for peptones.]

The rapidity of solution of fibrin is tested by placing fibrin, which is swollen up by the action of 0.2 per cent. HCl in a glass funnel, and adding the digestive fluid, observing the rapidity with which the fluid, the altered fibrin, drops from the funnel, and the fibrin disappears (*Grünhagen*). Or the fibrin may be coloured with carmine, swollen up in 0.1 per cent. HCl, and placed in the digestive fluid. The more rapidly the fluid is coloured red, the more energetic is the digestion.

Preparation.—Pure peptones are prepared by taking fluid which contains them and neutralising it with barium carbonate, evaporating upon a water-bath, and filtering. The barium is removed from the filtrate by the careful addition of sulphuric acid, and subsequent filtration.

Ptomaines.—Brieger extracted from gastric peptones by amylic alcohol a peptone-free poison, with actions like those of curare. It belongs to the group of *ptomaines*, i.e., alkaloids obtained from dead bodies or decomposing proteids. [Ptomaines are identical with the alkaloids in plants, and many have been isolated. The term *leucomaine* has been applied by Gautier to alkaloids formed by the decomposition of albuminous bodies during the normal metabolic processes taking place in the tissues. They are not formed by the activity of micro-organisms. Some seem to be formed in muscle, and are closely allied to creatin and xanthin (§ 250, IV.).]

Peptones are undoubtedly those modifications of albumin or proteids which, after their absorption from the intestinal canal into the blood, are destined to make good the proteids used up in the human organism. [It is important to note, however, that peptones are not found in the blood. They seem to be reconverted into some other proteid as they pass through the mucous membrane of the intestine towards the blood (§ 192).] By giving peptones (instead of albumin) as food life can not only be maintained, but there may even be an increase of the body-weight (*Plósz and Muly, Adamkiewicz*). Very probably, before being actually absorbed into the blood-stream, peptones are retransformed into serum-albumin or some closely allied body (§ 192).

Conditions affecting Gastric Digestion.—The presence of peptones already formed interferes with the action of the gastric juice, in so far as the greater concentration of the fluid interferes with and limits the mobility of the fluid-particles. Boiling, concentrated acids, alkali, and tannic acid, alkalinity of the gastric juice (e.g. by the admixture of much saliva), abolish the action; also sulphurous and arsenious acids and potassic iodide. The salts of the heavy metals, which cause precipitation with pepsin, peptone, and mucin, interfere with gastric digestion, and so do concentrated solutions of alkaline salts, common salt, magnesium and sodium sulphates. A small quantity of NaCl increases the secretion (*Grützner*) and favours the action of pepsin. Alkalies rapidly destroy pepsin, but less rapidly pro-pepsin (*Langley*). Alcohol precipitates the pepsin, but by the subsequent addition of water it is redissolved, so that digestion goes on as before. Any means that prevent the proteid bodies from swelling up, as by binding them firmly, impede digestion. Slightly over half a pint of cold water does not seem to disturb healthy digestion, but it does so in cases of disease of the stomach. Copious draughts of water, and violent muscular exercise, disturb digestion; while warm clothing, especially over the pit of the stomach, aids it. Menstruation retards gastric digestion. [Oddi finds that the presence of large quantities of ox bile, or even of its own bile in the stomach of a dog, does not affect the activity of the gastric juice, does not precipitate peptones, and does not excite vomiting (p. 348).]

[Artificial Digestion.]—The action of gastric juice on proteids may be observed outside the body, and we can prove, as is shown in the following table, after

Rutherford, that pepsin and an acid—*e.g.*, hydrochloric, along with water—are essential to the formation of gastric peptones:—

Beaker A.	Beaker B.	Beaker C.
Water. Pepsin, 0·3 per cent. Fibrin.	Water. HCl, 0·2 per cent. Fibrin.	Water. Pepsin, 0·3 per cent. HCl, 0·2 ,, Fibrin.
Keep all in water-bath at 38° C.		
Unchanged.	Fibrin swells up, becomes clear, and is changed into acid-albumin or syntonin.	Fibrin ultimately changed into peptone.

[In all animals, **gastric digestion** is essentially an **acid digestion**, and between the native proteid—fibrin, albumin, or any other form of proteid—and the end-product peptone there are numerous intermediate substances—protoses—the properties and characters of many of which have still to be investigated.]

[**Natural versus Artificial Digestion.**—It is to be remembered that there is a very great difference between natural and artificial digestion. In the former, the gastric juice is secreted all the time the food is present in the stomach, so that there is a favourable proportion of acid and ferment. Moreover, the movements of the stomach thoroughly mix the food with the digestive juice. The peptones are absorbed as they are formed or pass into the duodenum, so that they do not accumulate in the mixture and retard the process of digestion, as is the case in artificial digestion. It is obvious that as ordinarily conducted artificial digestion differs from normal digestion, *e.g.*, in the stomach, in the want of the following factors—the absence of (1) constant movements of the contents; (2) constant removal of the digestive products; and (3) continuous addition of fresh supply of digestive juice.]

[Kronecker and his pupils, Brink and Popoff, state that the gastric and intestinal mucous membrane can change gastric peptones into serum-albumin. The frog's heart can do the same, but much more slowly. The test applied for the conversion of peptone into serum-albumin was perfusion through the excised amphibian heart, which Kronecker regards as a very sensitive test for serum-albumin. A solution of peptone—which acts injuriously on the heart—when introduced into the stomach, or better, the intestine, of a dog, and then perfused through the heart, restores the latter after it has been exhausted by perfusion of normal saline.]

[**Exclusion of the Stomach.**—Ogata finds that if the stomach be divided at the pyloric end so as to exclude the stomach from the digestive apparatus, a dog can be nourished for a long time by introducing food through the pylorus into the duodenum. A dog has lived several years after excision of its stomach (*Czerny*). Raw flesh so introduced is digested more rapidly in the small intestine than in the stomach. The stomach not only digests, but it acts on the connective tissue of flesh so as to prepare the latter for intestinal digestion.]

II. Action on other Constituents of Food.—**Milk** coagulates or curdles when it enters the stomach, owing to the precipitation of the casein, and in doing so it entangles some of the milk-globules. [The curd is afterwards dissolved and digested by the gastric juice.] During the process of coagulation, heat is given off. The free hydrochloric acid of the gastric juice is itself sufficient to precipitate it; the acid removes from the alkali-albuminate or casein the alkali which keeps it in solution. Hammarsten separated a special ferment from the gastric juice—quite distinct from pepsin—the **milk-curdling ferment**, which, quite independently of the acid, precipitates the casein either in neutral or alkaline solutions. It is this ferment, or **rennet**, or **rennin**, which is used to coagulate casein in the making of cheese. [Rennin can curdle milk in a neutral solution, and neutralised gastric juice can do so also. The action of rennin is most active about 40° C., and its curdling action is destroyed by boiling.] Rennet is formed from a mother-substance in the chief cells of the gastric glands (p. 292). [Rennet is an infusion of the fourth stomach of the calf in brine (§ 231). The ferment which coagulates milk is quite distinct from pepsin. If magnesic carbonate be added to an infusion of calf's stomach, a precipitate is obtained. The clear fluid has strongly coagulating properties, while the precipitate is strongly peptic.]

The action of the milk-curdling ferment is perhaps, like the action of all ferments, a hydration of casein; it is greater in the presence of 0.2 HCl.

One part of the rennet-ferment can precipitate 800,000 parts of casein. When casein coagulates, two new proteids seem to be formed—the coagulated proteid which constitutes cheese, and a body resembling peptone dissolved in the whey—whey-proteid. The addition of calcium chloride accelerates, while water retards the coagulation (§ 231) (*Hammarsten*). [A ferment similar to rennet is contained in the seeds of *Withania coagulans* (*S. Lea*).]

Casein is first precipitated in the stomach, then a body like syntonin is formed, and finally peptone. During the process, a substance containing phosphorus and resembling nuclein appears (*Lubavin*).

[**Action of Acids versus Rennin on Milk.**—If a dilute acid be added to milk the casein is precipitated as such and not as a curd. It may even be re-dissolved and curdled with rennin. Casein may also be precipitated unchanged by neutral salts (NaCl, MgSO₄). The precipitate when washed can be redissolved in water in the presence of calcic phosphate, and this solution is coagulated by rennin. When casein is curdled by rennin, however, the casein is split up into two proteids—an insoluble one forming the **curd**, and a soluble one allied to albumin. The **curdling of milk** therefore seems to be due to the splitting up of a complex proteid by a ferment; one of the proteids is soluble, and closely allied to albumin—whey-proteid—the other is insoluble, and forms the curd: but this reaction will not take place—at least an insoluble curd will not be formed—if calcic phosphate be entirely absent. We are reminded of the analogous case of the coagulation of blood produced by the splitting up of fibrinogen in the presence of neutral salts.]

[Much confusion has existed regarding the terminology of the proteids in milk (§ 231). The chief proteid in milk, by some called casein, exists in milk partly dissolved and partly in suspension. The curd precipitated by rennin is quite insoluble in the whey. Some apply the term casein to the proteid which is present in milk, and curd to the insoluble casein produced by the ferment action of rennet. Halliburton proposes to call the proteid in milk **caseinogen**, and that which composes the curd **casein**. Foster calls the latter **tyrein**.]

There is a “**lactic acid ferment**” also present in gastric juice, which changes milk-sugar into lactic acid (*Hammarsten*). Part of the milk-sugar is changed in the stomach and intestine into grape-sugar.

Action on Carbohydrates.—Gastric juice does not act as a solvent of starch, inulin, or gums. Cane-sugar is slowly changed into grape-sugar. According to Uffelmann, the gastric mucus, and according to Leube, the gastric acid, are the chief agents in this process.

Action on Albumenoids and Fats—During the digestion of true cartilage, there is formed a chondrin-peptone, and a body which gives the sugar-reaction with Trommer's test. Perfectly pure elastin yields an elastin-peptone, similar to albumin-peptone, and hemi-elastin similar to hemi-albumose. A very minute quantity of **fat** is broken up into glycerin and fatty acids. [On neutral olive-oil being injected into the stomach of a dog, after several hours—the pylorus being plugged with an elastic bag—it partly splits up and yields oleic acid (*Cash and Ogata*).]

[We still require further observations on the gastric digestion of fats. Riche observed in his case of fistula, that fatty matters remained a long time in the stomach, and Ludwig found the same result in the dog. In some dyspeptics, rancid eructations often take place towards the end of gastric digestion.]

III. Action on the various Tissues.—(1) The **gelatin-yielding substance** (collagen) of all the connective-tissues (connective-tissue, white fibro-cartilage, and the matrix of bone), as well as gluten, is dissolved and peptonised by the gastric juice. [Gelatin, when acted on by gastric juice, no longer solidifies in the cold, but a **gelatin peptone** is formed, which is soluble and diffusible, although it differs from true peptone. In the dog, connective-tissues are specially acted on in the stomach, while the other parts of organs used as food are prepared for digestion in the small intestine, where the cellular and nuclear elements are digested by the pancreatic juice (*Bikfalvi*).] (2) The **structureless membranes** (*membranæ propriae*) of glands, sarcolemma, Schwann's sheath of nerve-fibres, capsule of the lens, the elastic laminae of the cornea, the membranes of fat-cells are dissolved, but the true elastic (fenestrated) membranes and fibres are not affected. (3) **Striped muscle**, after solution of the sarcolemma, breaks up transversely into discs, and, like non-striped muscle, is dissolved, and forms a true soluble

peptone, but parts of the muscle always pass into the intestine. (4) The albuminous constituents of the soft cellular elements of glands, stratified epithelium, endothelium, and lymph-cells, form peptones, but the nuclein of the nuclei does not seem to be dissolved. (5) The **horny parts** of the epidermis, nails, hair, as well as chitin, silk, conchiolin, and spongin of the lower animals, are indigestible, and so are amyloid-substance and wax. (6) The **red blood-corpuscles** are dissolved, the hæmoglobin decomposed into hæmatin and a globulin-like substance; the latter is peptonised, while the former remains unchanged, and is partly absorbed and transformed into bile-pigment. Fibrin is easily dissolved to form hœmi- and anti-peptone. (7) **Mucin**, which is also secreted by the goblet-cells of the stomach, passes through the intestines unchanged. (8) **Vegetable fats** are not affected by the gastric juice. Vegetable cells yield their protoplasmic contents to form peptones, while the **cellulose** of the cell-wall, in the case of man at least, remains undigested (§ 184). [(9) On **gluten-casein**, the chief proteid obtainable from wheaten flour or bread, artificial gastric juice yields soluble products or proteoses, or gluten-caseoses—which bear the same relation to the mother-substance as the albumoses of fibrin or albumin do to the mother-proteid. There is no essential difference in the general character of the proteids in this case between the animal and vegetable proteid. (*Chittenden and Smith*).]

Why the Stomach does not digest itself.—That the stomach can digest *living* things is shown by the following facts:—Bernard introduced the leg of a living frog through a gastric fistula into the stomach of a dog. Pavy did the same with the ear of a rabbit, and in both cases the objects introduced were digested. [Frenzel has modified this experiment, and shown that the legs of a living frog are digested by artificial gastric juice, the tissues being first killed and then digested. His experiments go to show that the alkalinity of the blood is not the protective medium.] The margins of a gastric ulcer and of gastric fistulae in man are attacked by the gastric juice. John Hunter (1772) discussed the question why the stomach does not digest itself. Not unfrequently after death the posterior wall of the stomach is found digested, [more especially if the person die after a full meal and the body be kept in a warm place, whereby the contents of the stomach may escape into the peritoneum. Cf. Bernard showed that if a rabbit be killed and placed in an oven at the temperature of the body, the walls of the stomach are attacked by its own gastric juice. Fishes also are frequently found with their stomach partially digested after death]. It would seem therefore, that, so long as the circulation continues, the tissues are protected from the action of the acid by the *alkaline* blood; this action cannot take place if the reaction be alkaline (*Pavy*). [This, however, does not explain why the pancreatic juice does not digest the pancreas.] Ligature of the arteries of the stomach causes digestive softening of the gastric mucous membrane. The thick layer of mucus may also aid in protecting the stomach from the action of its own gastric juice (*Cf. Bernard*). [Viola and Gaspardi find that if the spleen, with its circulation still intact, be introduced through a gastric fistula into the stomach of a dog, it is not digested even after 40 hours, but if the circulation was stopped it was reduced to a pulp in 8 hours. Here there is no question of the existence of columnar epithelium and a coating of mucus.]

[**Comparative.**—The process of gastric digestion seems to be essentially the same in all classes of vertebrates, with this exception, that while the gastric juice of mammals and birds is inactive at 0° C., that of cold-blooded animals is, although the optimum of the latter is 20° C. In the human foetus pepsin is formed shortly before birth, and according to Hammarsten, in the rabbit it is formed in the last week of intra-uterine life, and in the dog in the third week after birth. The formation of acid takes place much sooner.]

167. GASES IN THE STOMACH.—The stomach always contains a certain quantity of gas, derived partly from the gases swallowed with the saliva, partly from gases which pass backwards from the duodenum.

The air in the stomach is constantly undergoing changes, whereby its O is absorbed by the blood, and for 1 vol. of O absorbed 2 vols. of CO₂ are returned to the stomach from the blood. Hence, the amount of O in the stomach is very small, the CO₂ very considerable (*Plauer*).

Gases in the Stomach.—Vol. per cent. (*Plauer*).

Human Subject after Vegetable Diet.				Dog.	
		I.	II.	I. After Animal Diet.	II. After Legumes.
CO ₂ ,	. . .	20·79	33·83	25·2	32·9
H ₂ ,	. . .	6·71	27·58	...	...
N ₂ ,	. . .	72·50	38·22	68·7	66·3
O ₂ ,	. . .	...	0·37	6·1	0·8

By the acid of the stomach a part of the CO_2 is set free from the saliva, which contains much CO_2 (§ 146). The N acts as an indifferent substance.

Abnormal development of gases in persons suffering from gastric catarrh occurs when the gastric contents are *neutral* in reaction; during the butyric acid fermentation H and CO_2 are formed; the acetic acid and lactic acid fermentations do not cause the formation of gases. Marsh-gas (CH_4) has been found, but it comes from the intestine, as it can only be formed when no O is present (§ 184).

168. Structure of the Pancreas.—[The pancreas is a long, narrow, compound tubular gland of a cream colour and soft texture, which lies across the posterior wall of the abdomen behind the stomach and opposite the first lumbar vertebra (fig. 219). It is about 18 cm. long, 4 cm. broad, and 1.5 cm. thick, and weighs about 75 grams. The broader end or head lies in, and is embraced by the curvature of the

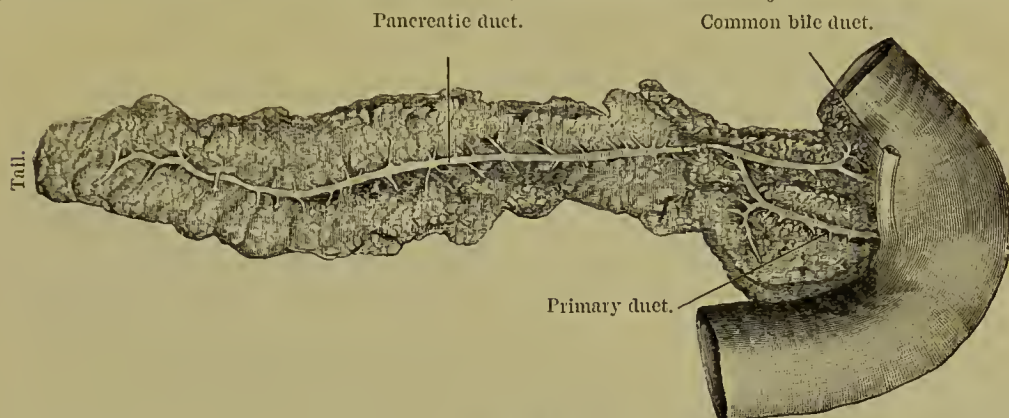


Fig. 219.

Pancreas and duodenum removed from the body, and seen from behind. The gland is cut to show the ducts.

duodenum, and the narrow end or tail is in contact with the spleen. The duct—**duct of Wirsung**—is about 2–3 mm. in diameter, runs along the whole length of the gland, and in its course it receives nearly at right angles contributory small ducts from the different lobules of the gland. It opens, along with the common bile-duct, into the duodenum, piercing the coats of the latter obliquely about 8 to 10 cm. below the pylorus. In man there is a small accessory duct—the **duct of Santorini**—opening independently into the duodenum. The gland has a thin connective-tissue capsule which sends a fine process and septa between its lobules, and these septa carry into it the blood-vessels and nerves. The **duct** consists of connective tissue, and is lined by a single layer of non-striated columnar or cylindrical cells. When traced backwards the ducts open into intermediate or intercalary parts lined by flattened epithelium, while the intercalary parts open into the acini.]

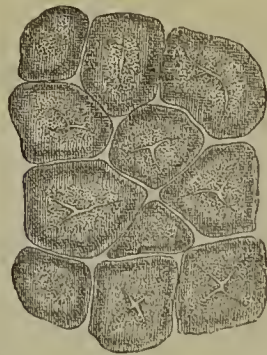


Fig. 220.

Section of the acini of fresh pancreas, showing the small lumen of the acini and the granular inner zone in the cells lining the acini.

The pancreas is a **compound tubular gland**, and in its general arrangement into **lobes**, **lobules**, and system of **ducts** and **acini**, it corresponds exactly to the true salivary glands (§ 142). The single layer of cylindrical epithelial cells lining the ducts is not at all, or only faintly, striated. The **acini** are tubular, or flask-shaped, and often convoluted. They consist of a *membrana propria*, resembling that of the salivary glands, lined by a single layer of somewhat cylindrical cells, with a more or less conical apex, directed towards the very narrow lumen of the acini. [As in the salivary glands, there is a narrow **intermediary part** of the ducts opening

into the acini, and lined by flattened epithelium. The acini are larger and more tubular than those of the salivary gland, and moreover, the acini are more numerous, so that in a section far fewer ducts are seen.]

[The cells lining the acini consist of **two zones** (fig. 220):—(1) The smaller **outer** or **parietal zone** in each cell is transparent, homogeneous, sometimes faintly striated, and readily stained with carmine and logwood; and (2) the **inner zone** (Bernard's granular layer) is granular, and stains but slightly with carmine (figs. 221, 222). [This inner zone contains a large number of more or less refractive granules depending on the state of physiological activity of the

gland (fig. 222).] It undoubtedly contributes to the secretion by giving off material, the granules being dissolved, while the zone itself becomes smaller. The spherical nucleus lies between the two zones. [The lumen of the acini is very small, and spindle-shaped or branched cells (**centro-acinar cells**) lie in it, and send their processes between the secretory cells, thus acting as *supporting cells* for the elements of the wall of the acini. During secretion there is a continuous change in the appearance of the cell-substance; the granules of the inner zone dissolve to form part of the secretion; new



Fig. 221.

Section of a pancreas stained with picro-carmin. D, duct; C, capsule; A, acinus (*Stirling*).

granules are formed in the homogeneous substance of the outer zone, and pass towards the inner zone (*Heidenhain, Kuhne, and Lea*).

[**Changes in the Cells during Digestion.**—When the cells are examined in the fresh condition, during the resting phase, or when the cells are “loaded,” they contain throughout their

substance a large number of refractive “granules” or spherules, which may obscure the nucleus. In the **active phase**, or in a “discharged” cell, the granules are far less numerous, they have disappeared from the outer zone of the cell, and are confined to its inner zone, and the relative width of the clear more or less homogeneous outer zone and that of the inner granular zone depends upon the activity of the cells, and the

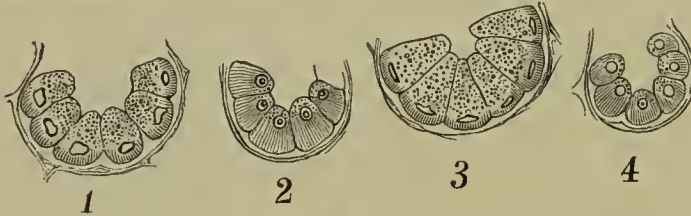


Fig. 222.

Changes of the pancreatic cells in various stages of activity. 1, During hunger; 2, in the first stage of digestion; 3, in the second stage; 4, during paralytic secretion.

greater the activity the fewer the granules in the inner zone. There is a close resemblance between the condition of the pancreatic cells and those of the serous salivary glands.] According to Heidenhain, during the *first* stage (6 to 10 hours) the granular inner zone diminishes in size, the granules disappear, while the striated outer zone increases in size (fig. 222, 2). In the *second* stage (10 to 20 hours) the inner zone is greatly enlarged and granular, while the outer zone is small (fig. 222, 3). During hunger the outer zone again enlarges (fig. 222, 1). In a gland where paralytic secretion takes place, the gland is much diminished in size, the cells are shrivelled (fig. 222, 4) and greatly changed. According to Ogata, some cells actually disappear during secretion (*Langley*).

The axially-placed excretory **duct** consists of an inner thick and an outer loose wall of connective and elastic tissues, lined by a single layer of columnar epithelium. Small mucous glands lie in the largest trunks. Non-medullated **nerves** with *ganglia* in their course, pass to the acini, but their mode of termination is unknown. [The nerves come from the semilunar ganglion along the splenic, gastro-duodenal

and superior mesenteric arteries.] The **blood-vessels** form a rich capillary plexus round some acini, while round others there are very few. It receives blood from several arteries (splenic, pancreatico-duodenal, and superior mesenteric), and its blood is returned to the portal system by the splenic and superior mesenteric veins.] Kühne and Lea found peculiar small cells in groups between the alveoli, and supplied with convoluted capillaries like **glomeruli**. Their significance is entirely unknown. [They are probably lymphatic in their nature.] The **lymphatics** resemble those of the salivary glands. [They begin as peri-vascular and peri-acinar spaces, and open into two lymphatic glands lying on the superior mesenteric artery. When a coloured injection is forced into the ducts under a high pressure, fine intercellular passages between the secreting cells are formed (*Saviotti's canals*), but they are *artificial* products.]

[**Number of Ducts.**—In making experiments upon the pancreatic secretion, it is important to remember that the number of pancreatic ducts varies in different animals. In man there is one duct opening along with the common bile-duct at Vater's ampulla, at the junction of the middle and lowest third of the duodenum. The rabbit has two ducts, the larger opening separately about 14 inches (30 to 35 cm.) below the entrance of the bile-duct (fig. 223). The dog and cat have each two ducts opening separately.]

Chemistry.—The *fresh* pancreas contains: water, proteids, ferments, fats, and salts. In a gland which has been exposed for some time, much leucin, isoleucin, butalin, tyrosin, often xanthin and guanin, are found; lactic and fatty acids seem to be formed from chemical decompositions taking place.

169. THE PANCREATIC JUICE.—**Method.**—Regner de Graaf (1664) tied a cannula in the pancreatic duct of a dog, and collected the juice in a small bag. Other experimenters made a **temporary fistula**. To make a **permanent fistula**, the abdomen is opened (dog), the pancreatic duct pulled forward, and stitched to the abdominal wall, with which it unites. Heidenhain cuts out the part of the duodenum where the duct opens into it, from its continuity with the intestine, and fixes it outside the abdominal wound.

The **secretion** obtained from a **permanent fistula** is a copious, slightly active, watery secretion, containing much sodium carbonate. The *thick* fluid obtained from the fistula before inflammation sets in, or that from a **temporary fistula**, acts far more energetically. This thick secretion, which is small in amount, is the *normal* secretion. The copious watery secretion is, perhaps, caused by the increased transudation from the dilated blood-vessels (possibly in consequence of the paralysis of the vaso-motor nerves). It is, therefore, in a certain sense, a “paralytic secretion” (§ 145). The **quantity** varies much, according as the fluid is thick or thin. During digestion, a large dog secretes 1 to 1·5 gram. of a thick secretion (*Cl. Bernard*). Bidder and Schmidt obtained in twenty-four hours 35 to 117 grams of a watery secretion per kilo. of a dog. When the gland is not secreting, and is **at rest**, it is soft, and of a pale yellowish-red colour, but **during secretion** it is red and turgid with blood, owing to the dilatation of the blood-vessels. [It is to be remembered that most of the experiments have been made in the pancreatic juice of the dog.]

Physical and Chemical Characters of the Secretion.—The **normal secretion** is thick, transparent, colourless, odourless, saltish to the taste, and has a strong **alkaline** reaction, owing to the presence of sodium carbonate, so that when an acid is added, CO_2 is given off. It contains several groups of substances—(1) *serum*—

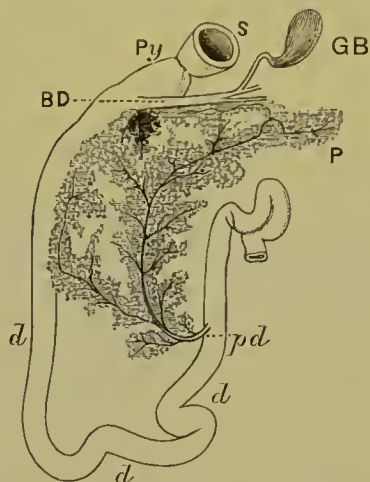


Fig. 223.

Pancreas of the rabbit P; *pd*, pancreatic duct; *d, d*, duodenum; *Py*, pylorus; *S*, stomach; *GB*, gall-bladder; *BD*, bile-duct.

albumin and alkali-albuminate; it is sticky, somewhat viscid, flows with difficulty, and is coagulated by heat into a white mass. In the cold, there separates a jelly-like albuminous coagulum. Nitric, hydrochloric, and sulphuric acids, cause a precipitate; while the precipitate caused by alcohol is redissolved by water. (2) *Several ferments* (p. 304); (3) *Nitrogenous bodies*, e.g., leucin, guanin, etc., in small amount; (4) *Traces of soaps*; (5) *Salts*, less than 1 per cent. Cl. Bernard found in the normal pancreatic juice of a dog 8.2 per cent. of organic substances, and 0.8 per cent. of ash. The juice (dog) analysed by Carl Schmidt contained in 1000 parts:—

	Collected on first opening the duct.	Permanent Fistula.
Water, ...	900.8	979.0
Solids, ...	99.2	20.0
Solids { Organic Matter, ...	90.4	12.4
{ Inorganic ,, ...	8.8	7.6

The ash from 1000 parts of juice yielded—

Soda, ...	0.58	3.32
Sodic chloride, ...	7.35	2.50
Potassic chloride, ...	0.02	0.93
Phosphates of alkaline earths and iron, ...	0.53	0.08
Sodic phosphate, ...	...	0.01
Lime and magnesia, ...	0.32	0.01

The more rapid and more profuse the secretion, the poorer it is in organic substances, while the inorganic remain almost the same; nevertheless, the total quantity of solids is greater than when the quantity secreted is small (*Bernstein*). Traces of **leucin** and **soaps** are present in the fresh juice. [It usually contains few or no structural elements. Any structural elements present in the fresh juice, as well as its proteids, are digested by the peptone-forming ferment of the juice, especially if the latter be kept for some time. If the fresh juice is allowed to stand for some time, and then mixed with chlorine water, a red colour is obtained.]

Concretions are rarely formed in the pancreatic ducts; they usually consist of calcic carbonate. Dextrose has been found in the juice in diabetes, and urea in jaundice. Schiff's statement that the pancreas secretes only after the absorption of dextrin has not been confirmed. The secretory activity of the pancreas is not dependent on the presence of the spleen.

[**Comparative.**—The pancreatic juice of the dog contains about 10 per cent. of solids; of these 9 is organic, 1 mineral. In other animals, however, the percentage of solids is much less; in the sheep 2.15, and rabbit 1.76. Herter found over 20 per cent. of solids in the fluid accumulated in a human dilated pancreatic duct. In many fishes the pancreatic juice is acid, and does not contain any diastatic ferment. In molluscs and arthropoda there is a ferment analogous to trypsin. The secretion is intermittent in carnivora and continuous in herbivora.]

170. ACTIONS OF THE PANCREATIC JUICE.—The presence of **four enzymes**, or **hydrolytic ferments**, makes the pancreatic juice one of the most important digestive fluids in the body.

I. Its **diastatic action** is due to the diastatic ferment **amyllopsin**, a substance which seems to be identical with the saliva ferment; but it acts much more energetically than the ptyalin of saliva on *raw* starch as well as upon boiled starch; at the temperature of the body the change is effected almost at once, while it takes place more slowly at a low temperature, **maltose** being formed. Glycogen is changed into dextrin and grape sugar; and achroodextrin into sugar. Even cellulose is said to be dissolved, and gum changed into sugar by it, but inulin remains unchanged.

[If digestion of starch by pancreatic juice or saliva be carried on under conditions approximating as nearly as possible to those existing in the intestine, nearly the whole of the starch may be converted into maltose, there being but little dextrin left at the end of a prolonged digestion. The presence of the maltose seems to prevent

the further conversion of the small remainder of dextrin into sugar (*Sheridan Lea*). **Sugar** seems to be the final form in which the products of digestion of carbohydrates leave the intestine and pass into the blood.]

According to v. Mering and Musculus, the starch (as in the case of the saliva, § 148) is changed into maltose, and a reducing-dextrin; so also is glycogen. Amylopsin changes achroodextrin into maltose; at 40° C. maltose is slowly changed into dextrose, but cane-sugar is not changed into invert-sugar. The ferment is precipitated by alcohol, while it is extracted by glycerin without undergoing any essential change. All conditions which destroy the diastatic action of saliva (§ 148) similarly affect its action, but the admixture with acid gastric juice (its acid being neutralised) or bile does not seem to have any injurious influence. This ferment is absent from the pancreas of new-born children (*Korowin*).

Preparation of the ferment.—It is isolated by the same methods as obtain for ptyalin (§ 148), but the tryptic ferment is precipitated at the same time. The addition of neutral salts (4 per cent. solution), *e.g.*, potassium nitrate, common salt, ammonium chloride, increases the diastatic action.

II. Its **tryptic** or **proteolytic action**, or its action on proteids, depends upon the presence of a hydrolytic ferment which is now termed **trypsin** (*Kühne*). Trypsin acts upon proteids at the temperature of the body, when the reaction is *alkaline*, and changes them first into a globulin-like substance, then into propeptone or albumose, and lastly into a *true peptone*, sometimes called tryptone. The albumoses are not so abundant or so easily separated as in gastric digestion (see also p. 295); [as in gastric digestion the peptones formed are **hemi-peptone** and **anti-peptone**, but the former alone undergoes further change when it is acted on by the pancreatic juice]. The proteids do not swell up before they are changed into peptone, [but they are eroded or eaten away by the action of the juice]. When the proteid has been previously swollen up by the action of an acid, or when the reaction of the medium is acid, the transformation is interfered with, although the changes go on slowly in a neutral medium.

Substances yielding gelatin, nuclein (?), and Hb, resist trypsin; glutin and swollen-up gelatin-yielding substances are changed into gelatin-peptone, but the latter undergoes no further change. Hb-O₂ is split up into albumin and hæmochromogen. In other respects, trypsin acts on tissues containing albumins just like pepsin (§ 166, III.).

Trypsin is never absent from the pancreas of **new-born children** (*Zweifel*), and it may be extracted by water, which, however, also dissolves the albumin. Kühne has carefully separated the albumin and obtained the ferment in a pure state. It is soluble in water, insoluble in alcohol. Pepsin and hydrochloric acid together act upon trypsin and destroy it; hence it is not advisable to administer trypsin by the mouth, as it would be destroyed in the stomach. When dried it may be heated to 160° without injury.

Trypsin is formed within the pancreas by a "**mother-substance**," or **zymogen**, taking up oxygen. The zymogen is found in small amount, 6 to 10 hours after a meal, in the inner zone of the secretory cells, but after 16 hours it is very abundant in the inner zone of the cells. It is soluble in water and glycerin. Trypsin is formed in the watery solution from the zymogen, and the same result occurs when the pancreas is chopped up and treated with strong alcohol (*Kühne*). The addition of sodium chloride, carbonate, and glycocholate, favours the activity of the tryptic ferment (*Heidenhain*). [The following facts show that zymogen (ζύμη, ferment), or, as it has been called, **trypsinogen**, is the precursor of trypsin, that it exists in the gland-cells, and requires to be acted upon before trypsin is formed. If a glycerin extract be made of a pancreas taken from an animal just killed, and if another extract be made from a similar pancreas which has been kept for 24 hours, it will be found that an alkaline solution of the former has practically no effect on fibrin, while the latter is powerfully proteolytic. If a fresh, and still warm, pancreas be rubbed up with an equal volume of a 1 per cent. solution of acetic acid, and then extracted with glycerin, a powerfully proteolytic extract is at once obtained. Trypsin is formed from zymogen by the action of acetic acid. There is reason to believe that trypsin is formed from zymogen by oxidation, and that the former loses its proteolytic power after removal of its oxygen. The

amount of zymogen present in the gland-cells seems to depend upon the number and size of the granules present in the inner granular zone of the secretory cells.]

Further Effects on Proteids.—When **trypsin** is allowed to act upon the **hemi-peptone** formed by its own action, the latter is partly changed into the amido-acid, **leucin**, or **amido-caproic acid** ($C_6H_{13}NO_2$), and **tyrosin** ($C_9H_{11}NO_3$). Tyrosin belongs to the aromatic series (§ 252, IV. 3). Hypoxanthin, xanthin, and aspartic or amido-succinic acid ($C_4H_7NO_4$) are also formed during the digestion of fibrin and gluten, and so are glutamic ($C_5H_9NO_4$) and amido-valerianic acid ($C_5H_{11}NO_2$). *Gelatin* is first changed into a gelatin-peptone, and afterwards is decomposed into *glycin* and ammonia.

Putrefactive Phenomena.—If the action of the pancreatic juice be still further prolonged, especially if the reaction be alkaline, a body with a strong, stinking, disagreeable faecal odour is formed together with **indol** (C_8H_7N), **skatol** (C_9H_9N), and **phenol** (C_6H_6O), and a substance—**protein-chromogen**—which becomes red on the addition of chlorine-water (*Bernard*), [or it gives with bromine-water first a pale red and then a violet tint (*Kühne*)], volatile fatty acids are formed, while, at the same time, H , CO_2 , H_2S , CH_4 , and N are given off. The formation of indol and the other substances just mentioned depends upon **putrefaction** (§ 184, III.). Their formation is prevented by the addition of salicylic acid, or thymol, which kills the organisms upon which putrefaction depends (*Kühne*).

[Peptones are formed from proteids by the action of the pancreatic ferment without the aid of micro-organisms (if the digestive fluid contains 1 per cent. carbolic acid it is quite anti-septic). The production of indol is always associated with the appearance of micro-organisms in the medium, and Harris and Tooth incline to the view that there are special indol-forming organisms, in the absence of which this body does not appear.]

[Artificial Digestion and Pancreatic v. Gastric Digestion.]—From fibrin placed in pancreatic juice, or in a 1 per cent. solution of sodium carbonate containing the ferment trypsin, peptones are rapidly formed at $40^\circ C$. When we **compare gastric with pancreatic digestion**, we find that the fibrin in pancreatic digestion is eroded, or eaten away, and never swells up. The process takes place in an alkaline medium, and never in an acid one. In fact, a 1 per cent. solution of sodic carbonate seems to play the same part in assisting trypsin that a 2 per cent. solution of HCl does for pepsin, in gastric digestion. In gastric digestion acid-albumin or *syntonin* is formed in addition to the true peptones. In pancreatic digestion a body resembling *alkali-albumin*, which passes into a globulin-like body, and ultimately into a peptone, is formed. Of the peptones so produced, one is called **anti-peptone**, and it is not further changed, but part of the proteid is changed into **hemi-peptone**. This body, when acted upon, yields **leucin** and **tyrosin**. When putrefaction takes place, the bodies above-mentioned are also formed. We might represent the action of trypsin thus:—Proteid + trypsin + 1 per cent. sodium carbonate, kept at $38^\circ C$. = formation of a globulin-like body, and then anti-peptone and hemi-peptone are formed.

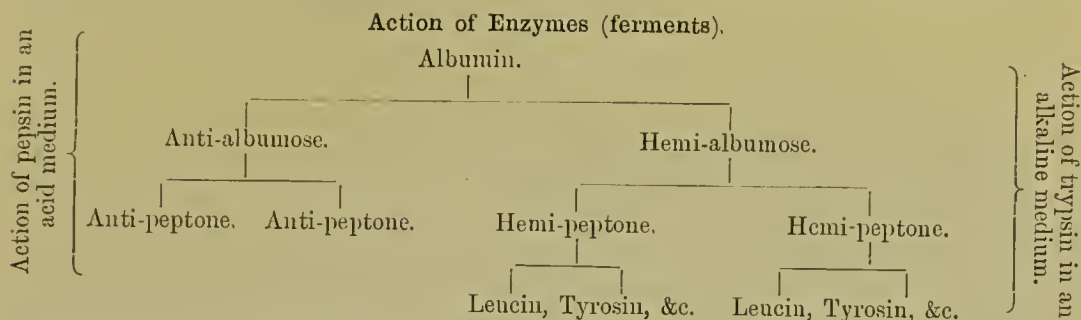
Anti-peptone	Hemi-peptone		
	yields	yields	
	Normal Digestive Products.	Putrefactive Products.	
undergoes no further change.	Leucin, Tyrosin, Hypoxanthin, Aspartic Acid.	Indol, Skatol, Phenol.	Volatile Fatty Acids, H , CO_2 , H_2S , CH_4 , N .

It seems that trypsin in pure water can act slowly upon fibrin to produce peptone. Pepsin cannot do this without the aid of an acid.]

[In artificial tryptic digestion of fibrin Kühne obtained 9.1 per cent. of leucin

and 3.86 of tyrosin. S. Lea more recently obtained 8–10 per cent. of the former, and 2–3 per cent. of the latter—*i.e.* in the ratio of 3 : 1. Lea confirms Kühne's view, and has further shown from the examination of the contents of the duodenum in a dog after digestion of a meal of flesh, that both leucin and tyrosin are formed in the intestine in not inconsiderable quantities during natural tryptic digestion.]

[The following scheme by Kühne indicates the action of ferments (and certain acids) on proteids. The latter are split up into an anti-group and a hemi-group.



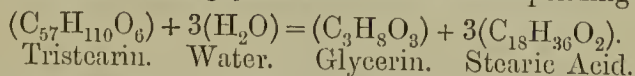
The anti-group is not further split up but the hemi-group although not split up by gastric digestion, is split up by tryptic digestion into leucin, tyrosin, and other products.]

[Kühne's Pancreas Powder.—This is prepared by the prolonged extraction of fresh pancreas of ox with alcohol and then with ether. If the dry powder be extracted for several hours with a 1 per cent. solution of salicylic acid, and filtered, a fluid with powerful proteolytic, but no diastatic, properties is obtained. Several hours afterwards much tyrosin may separate out, which, of course, must be removed by filtration. The clear fluid, when mixed with fibrin and a 1 per cent. solution of sodic carbonate, rapidly digests fibrin. If it be desired to obtain a true pancreatic digestion, with none of the products of putrefaction, the mixture must be strongly "thymolised" with a 25 per cent. alcoholic solution of thymol (*Kühne*).]

[Setschenow finds that egg-albumin, boiled in a vacuum at 35°–40° C., is more rapidly digested than fibrin by a specially prepared trypsin.] When proteids are boiled for a long time with dilute H₂SO₄, we obtain peptone, then *leucin* and *tyrosin*; gelatin yields *glycin*. Hypoxanthin and xanthin are obtained in the same way by similarly boiling fibrin, and the former may even be obtained by boiling fibrin with water (*Chittenden*).

It is very remarkable that the juice of the green fruit of the papaya tree, or *Carica papaya*, possesses digestive properties (*Roy, Wittmack*), and that the action is due to a peptonising ferment, closely related to trypsin, and called *caricin* or *papain*. [It forms a true peptone, an intermediate body, and leucin and tyrosin. It also contains a milk-coagulating ferment (*Martin*).] The milky juice of the fig-tree has a similar action. Sprouting malt, vetch, hop, hemp during sprouting, and the receptacle of the artichoke contain a peptonising ferment. Leucin, tyrosin, glutamic and aspartic acids, and xanthin are formed in the seeds of some plants; hence we may assume that the processes of decomposition in some seeds are closely allied to the fermentative actions that occur in the intestine.

III. Its action on neutral fats is twofold:—(1) It acts upon fats so as to form a fine permanent emulsion. (2) It causes neutral fats to take up a molecule of water and split into glycerin and their corresponding fatty acids:—



The latter result is due to the action of an easily-decomposable fat-splitting ferment (*Cl. Bernard*), also called **steapsin**. Lecithin is decomposed by it into glycerin-phosphoric acid, neurin, and fatty acids. The fatty acids thus liberated are partly *saponified* by the alkali of the pancreatic and intestinal juices, and partly emulsified by the alkaline intestinal juice. Both the soaps and emulsions are capable of being absorbed (§ 191).

Emulsification.—The most important change effected on fats in the small intestine is the production of an emulsion, or their subdivision into exceedingly minute particles (§ 191). This

is necessary in order that the fats may be taken up by the lacteals. If the fat to be emulsified contain a free fatty acid, *i.e.*, if it be slightly rancid, and if the fluid with which it is mixed be *alkaline*, emulsification takes place extremely rapidly (*Brücke*). A drop of cod-liver oil, which in its unpurified condition always contains fatty acids, on being placed in a drop of 0.3 per cent. solution of soda, instantly gives rise to an emulsion (*Gad*). The excessively minute oil-globules that compose the emulsion are first covered with a layer of soap, which soon dissolves, and in the process small globules are detached from the original oil-globules. The fresh surface is again covered by a soap film, and the process is repeated over and over again until an excessively fine emulsion is obtained. If the fat contain much fatty acid, and the solution of soda be more concentrated, "*myelin forms*" are obtained similar to those which are formed when fresh nerve-fibres are teased in water. Animal oils emulsionise more readily than vegetable oils; castor oil does not emulsionise (*Gad*). [It is extremely difficult to obtain a perfectly neutral oil, as most oils contain a trace of a fatty acid. In fact, if on adding a weak solution of sodic carbonate to oil or fatty matters, fluid at the temperature of the body, an emulsion is obtained, one may be sure that the oil contained a fatty acid, so that Bernard's view about an "emulsive ferment" being necessary is not endorsed. The fatty acid set free by the fat-splitting ferment enables the alkaline pancreatic juice at once to produce an emulsion.]

Fat-Splitting Ferment.—This is a very unstable body, and must be prepared from the perfectly fresh gland by rubbing it up with powdered glass, glycerin, and a 1 per cent. solution of sodic carbonate, and allowing it to stand for a day or two (*Grützner*). [This ferment is said to cause an emulsion of oil and mucilage tinged blue with litmus at 40° C. to become red (*Gaenger*). In performing this experiment notice that the mucilage is perfectly neutral, as gum-arabic is frequently acid.]

[Pancreatic Extracts.]—The action of the pancreas may be tested by making a watery extract of a perfectly fresh gland. Such an extract always acts upon starch and generally upon fats, but this extract and also the glycerin extract vary in their action upon proteids at different times. If the extract—watery or glycerin—be made from the pancreas of a fasting animal, the tryptic action is slight or absent, but is active if it be prepared from a gland 4 to 10 hours after a meal. The pancreatic preparations of Benger of Manchester, Savory and Moore, or Burroughs and Wellcome, all possess active diastatic and proteolytic properties.]

[Pancreas Ferments.]—Finely divided calf's pancreas is extracted with less than twice its volume of water and kept for five hours at 38° C. The fluid is decanted, shaken with ether, and precipitated with alcohol. The precipitate is spread on filter paper and dried at 40° C. A small piece of this paper extracted with 3–4 cc. of water yields a fluid with diastatic, tryptic, and it is said, fat-splitting activities (*Setschenow*).]

[Pancreas Salt.]—Prosser James proposes to employ common salt mixed with pepsin, which he calls peptic salt; and he advocates the use of another preparation composed of the pancreatic ferments and common salt, pancreatic salt.]

The pancreas of **new-born children** contains trypsin and the fat-decomposing ferment, but not the diastatic one (*Zweifel*). A slight diastatic action is obtained after two months, but the full effect is not obtained until after the first year (*Korowin*).

IV. The pancreas contains a **milk-curdling ferment**, which may be extracted by means of a concentrated solution of common salt.

171. THE SECRETION OF THE PANCREATIC JUICE.—**Rest and Activity.**—As in other glands, we distinguish a quiescent state, during which the gland is soft and pale, and a state of secretory activity, during which the organ swells up and appears pale red. The latter condition only occurs after a meal, and is caused probably reflexly owing to stimulation of the nerves of the stomach and duodenum. Kühne and Lea found that all the lobules of the gland were not active at the same time. The pancreas of the herbivora secretes uninterruptedly, [but in the dog secretion is not constant].

Time of Secretion.—According to Bernstein and Heidenhain the secretion begins to flow when food is introduced into the stomach, and reaches its maximum 2 to 3 hours thereafter. The amount falls towards the 5th or 7th hour, and rises again (owing to the entrance of the chyme into the duodenum) towards the 9th and 11th hour, gradually falling towards the 17th to 24th hour until it ceases completely. When more food is taken, the same process is repeated. As a general rule, a rapidly-formed secretion contains less solids than one formed slowly.

Condition of Blood-Vessels.—During secretion, the blood-vessels behave like

the blood-vessels of the salivary glands after stimulation of the chorda—they dilate, and the venous blood is bright red—thus, it is probable that a similar nervous mechanism exists, [but as yet no such mechanism has been discovered]. The secretion is excreted at a pressure of more than 17 mm. Hg. (rabbit).

Effect of Nerves.—The nerves arise from the hepatic, splenic, and superior mesenteric plexuses, together with branches from the vagus and sympathetic. The secretion is **excited** by stimulation of the medulla oblongata, as well as by direct stimulation of the gland itself by induction-shocks. [It is not arrested by section of the cervical spinal cord.] The secretion is **suppressed** by **atropin** [in the dog, but not the rabbit], by producing vomiting, by stimulation of the central end of the vagus, as well as by stimulation of other sensory nerves, *e.g.*, the erual and sciatic. Extirpation of the nerves accompanying the blood-vessels prevents the above-named stimuli from acting. Under these circumstances, a thin “**paralytic secretion**,” with feeble digestive powers, is formed, but its amount is not influenced by the taking of food. [Secretion is excited by the injection of ether into the stomach.]

Excision of the Pancreas.—The duct may be ligatured in animals, without causing any very great change in their nutrition; the absorption of fat from the intestine does not cease. After the duct is ligatured it may be again restored. Ligature of the duct may cause the formation of cysts in the duct and atrophy of the gland-substance. Pigeons soon die after this operation. [After excision of the pancreas, dogs become permanently diabetic (p. 323). There may be as much as 5–10 per cent of sugar in the urine during fasting. In the later stages before death acetonuria occurs (*Minkowski and v. Mering*).]

[**172. PREPARATION OF PEPTONISED FOOD.**—Peptonised food may be given to patients whose digestion is feeble (*Roberts*). Food may be peptonised either by peptic or tryptic digestion, but the former is not so suitable as the latter, because in peptic digestion the grateful odour and taste of the food are destroyed, while bitter by-products are formed, so that pancreatic digestion yields a more palatable and agreeable product. As trypsin is destroyed by gastric digestion, obviously it is useless to give extract of the pancreas to a patient along with his food.]

[**Peptonised Milk.**—“A pint of milk is diluted with a quarter of a pint of water and heated to 60° C. Two or three tea-spoonfuls of Benger’s liquor pancreaticus, together with 10 or 20 grains of bicarbonate of soda, are then mixed therewith.” Keep the mixture at 38° C. for about two hours, and then boil it for two or three minutes, which arrests the ferment action.]

[**Peptonised Gruel**, prepared from oatmeal, or any farinaceous food, is more agreeable than peptonised milk, as the bitter flavour does not appear to be developed in the pancreatic digestion of *vegetable* proteins.]

[**Peptonised Milk-Gruel** yielded Roberts the most satisfactory results, as a complete and highly nutritious food for weak digestions. Make a thick gruel from any farinaceous food, *e.g.*, oatmeal, and while still hot add to it an equal volume of cold milk, when the mixture will have a temperature of 52° C. (125° F.). To each pint of this mixture add two or three tea-spoonfuls of liquor pancreaticus and 20 grains of bicarbonate of soda. It is kept warm for two hours under a “cosey.” It is then boiled for a few minutes and strained. The bitterness of the digested milk is almost completely covered by the sugar produced during the process.]

[Peptonised soups and beef-tea have also been made and used with success, and have been administered both by the mouth and rectum.]

[**Peptonising powders** containing the proper proportions of ferment and sodic bicarbonate are prepared by Benger, and Burroughs and Wellcome.]

[**173. Structure of the Liver.**—The liver is the heaviest organ in the body, weighing in the adult, when devoid of blood, about 1850 grams. It forms $\frac{1}{10}$ of the weight of the male body, and is about 28 cm. in length, 18 cm. in breadth at its thickest part. The bile is carried out of the liver by the two **hepatic ducts**, which emerge from the right and left hepatic substance at the transverse fissure. They unite and are joined by the **cystic duct**, which is a continuation of the tapering extremity of the gall-bladder. By the union of the hepatic duct with the cystic duct the **common bile duct** (75 mm. long) is formed. It pierces the

coats of the duodenum very obliquely, and opens, along with the pancreatic duct, into the duodenum. The **gall-bladder** is a pear-shaped sac, capable of containing

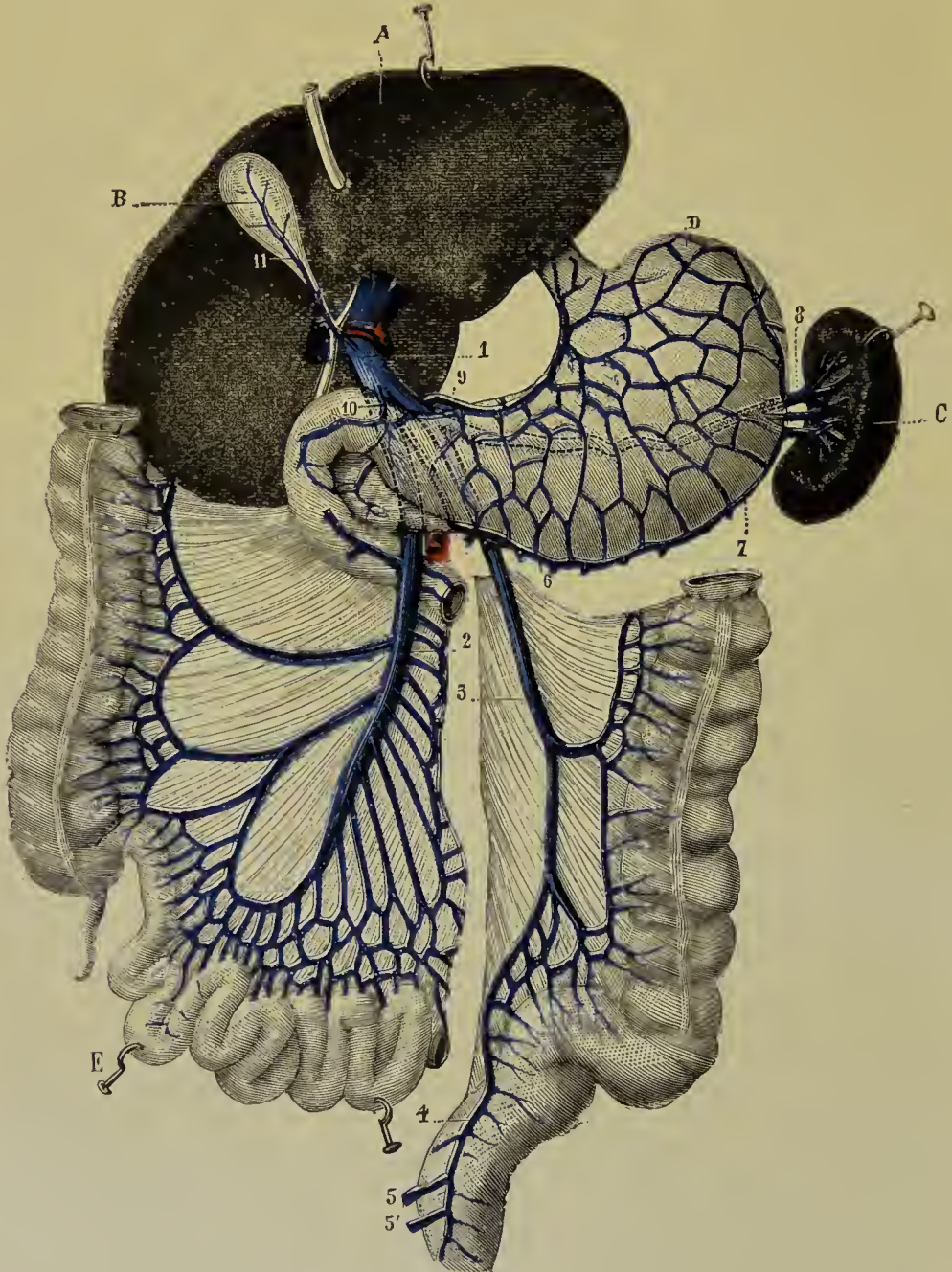


Fig. 224.

Portal vein and its branches of origin. A, liver; B, gall-bladder; C, spleen; D, stomach; E, part of the small intestine; 1, trunk of the portal vein; 2, superior and 3, inferior mesenteric veins; 4, superior, 5, 5', middle and inferior hæmorrhoidal veins; 6, right, and 7, left, gastro-epiploic veins; 8, splenic vein; 9, gastric coronary vein; 10, pyloric vein; 11, cystic vein.

20–25 c.c. of bile. In some animals the gall-bladder is wanting, as in the donkey, elephant, and mouse.]

[**Blood-Vessels of the Liver.**—The liver is supplied with blood by

- (1) The portal vein. (2) The hepatic artery.

The **portal vein** is formed by the confluence of the splenic, inferior, and superior mesenteric veins, whereby the short, wide vena portæ is formed (fig. 224, 1). It enters the liver at the transverse fissure, accompanied by the bile-duct and hepatic artery, and is distributed between the liver lobules. The portal vein returns the blood from the stomach, pancreas, intestines, and spleen; hence it carries some of the products of digestion directly to the liver, where some of them are materially changed by the hepatic cells as they pass slowly through the hepatic blood-vessels. The **hepatic artery** supplies a small quantity of arterial blood to the liver. The blood, after circulating through the liver, is returned by the **hepatic veins** to the inferior vena cava.]

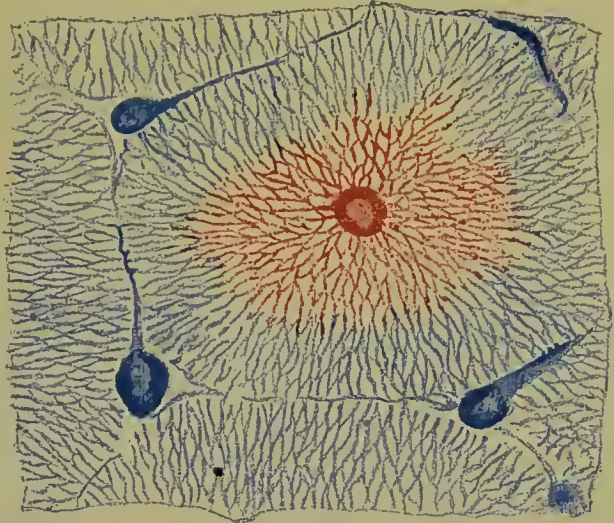


Fig. 225.

Blood-vessels of a rabbit's liver injected; portal vein, blue; hepatic vein, red (*Stirling*).

The **liver** consists of innumerable small **lobules** or **acini**, 1 to 2 millimetres in diameter. These lobules are visible to the naked eye. All the lobules have the same structure.

1. **The Capsule.**—The liver is covered by a thin, fibrous, firmly-adherent capsule, which has on its free surface a layer of endothelium derived from the peritoneum. The capsule sends fine septa into the organ between the lobules, but it is also continued into the interior at the transverse fissure, where it surrounds the portal vein, hepatic artery, and bile-duct, and accompanies these structures as the **capsule of Glisson**, or interlobular connective tissue. The spaces in which these three structures lie are known as **portal canals**. In some animals (pig, camel, polar bear) the lobules are separated from each other by the somewhat lamellated connective tissue of Glisson's capsule, but in man this is but slightly developed, so that adjoining lobules are more or less fused. Very delicate connective tissue, but small in amount, is

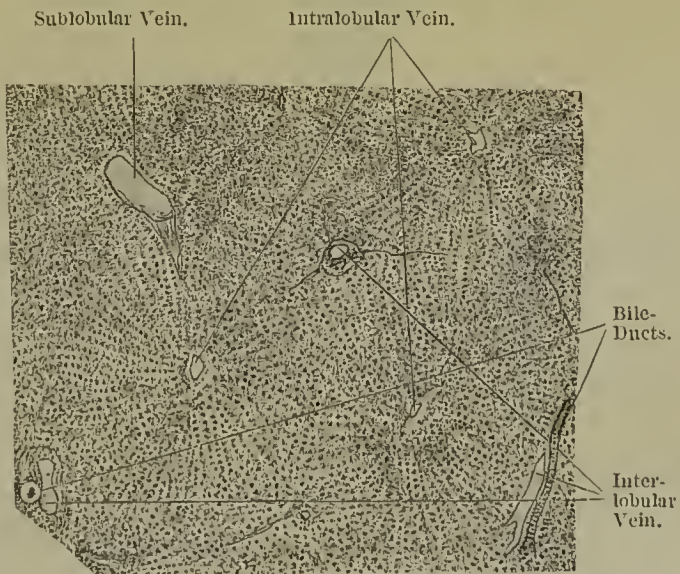
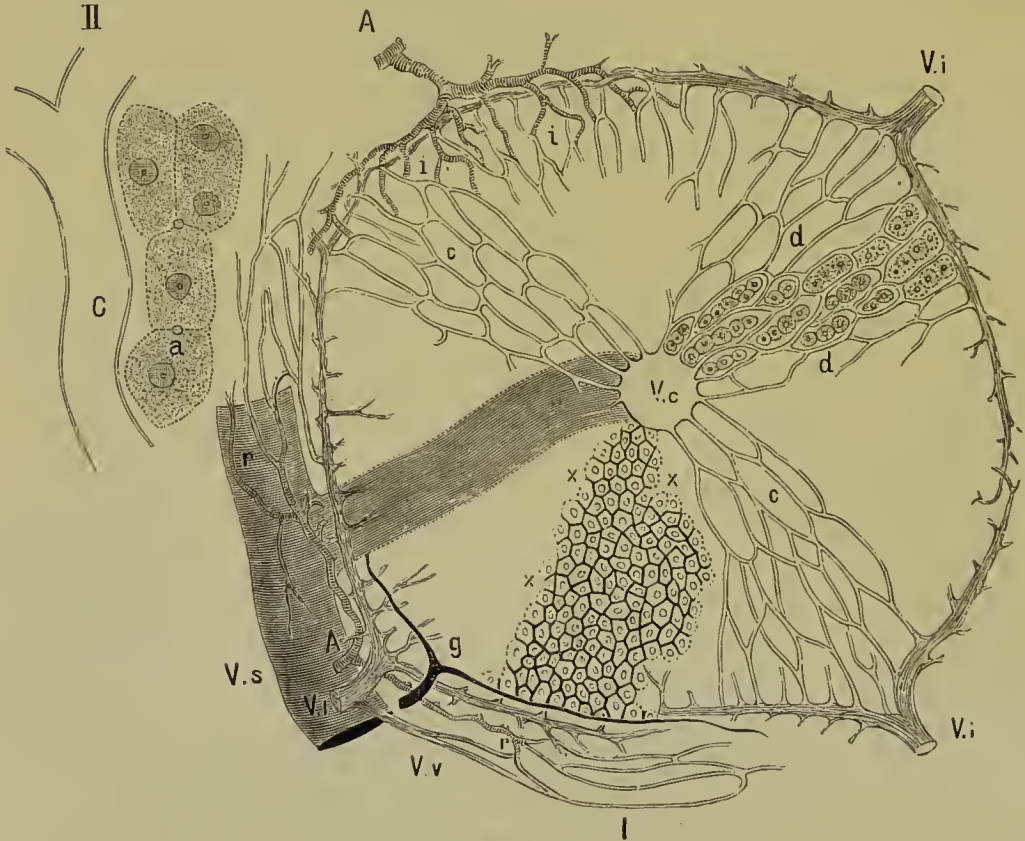


Fig. 226.

Section of human liver, $\times 20$, showing the liver-lobules and the radiate arrangement of their cells from the central or intralobular vein.

also found within the lobules. Leucocytes are sometimes found in the tissue of Glisson's capsule.

2. **Blood-Vessels**—(a) **Branches of the Venous System**.—The **portal vein**, after its entrance into the liver at the portal fissure, gives off numerous branches lying **between the lobules**, and ultimately forming small trunks which reach the periphery of the lobules, where they form a rich plexus. The branches of the portal vein lying between the lobules are called the **interlobular veins** (figs. 225, 226, 227, *V.i.*), which are always provided with thick muscular walls. From



[Fig. 227.]

I, Scheme of a liver-lobule—*V.i*, *V.i*, interlobular vein (portal); *V.c*, central or intralobular vein (hepatic); *c, c*, capillaries between both; *V.s*, sublobular vein; *V.v*, vena vascularis; *A, A*, hepatic artery, giving branches, *r, r*, to Glisson's capsule and the larger vessels, and ultimately forming the *venæ vasculares* at *i, i*, opening into the intralobular capillaries; *g*, bile-duets; *x, x*, intralobular biliary channels between the liver-cells; *d, d*, position of the liver-cells between the meshes of the blood-capillaries. II. Isolated liver-cells—*c*, a blood-capillary; *a*, fine bile-capillary channel.

these veins numerous **capillaries** (*c, c*) are given off to the entire periphery of the lobule. The capillaries converge towards the centre of the lobule. As they proceed inwards, they form elongated meshes, and between the capillaries lie rows or columns of liver-cells (*d, d*). The capillaries are relatively wide, and are so disposed as to lie between the *edges* of the columns of cells, and never between the surfaces of two neighbouring cells. The capillaries converge towards the centre of each lobule, where they join to form one large vein, the **intralobular, hepatic, or central vein** (*V.c*), which traverses each lobule, reaches its surface at one point, passes out, and joins similar veins from other lobules to form the **sublobular veins** (fig. 227, *V.s*). The branches of the hepatic veins have very thin walls.

These in turn unite to form wide veins, the origins of the **hepatic vein**, which opens into the vena cava inferior.

(b) The branches of the **hepatic artery** accompany the branches of the portal vein and bile-duct in the portal canals between the lobules, and in their course give off capillaries to supply the walls of the portal vein and larger bile-ducts. The branches of the hepatic artery anastomose frequently where they lie between the lobules. On reaching the periphery of the lobules, a certain number of capillaries are given off, which penetrate the lobule, and terminate in the capillaries of the portal vein (*i, i*). These capillaries, however, which supply the walls of the portal vein and large bile-ducts (*r, r*), terminate in veins which end in the portal vein (*V.v*). Several branches—*capsular*—pass to the surface of the liver, where they form a wide-meshed plexus under the peritoneum. The blood is returned by veins, which open into branches of the portal vein.

[**Hepatic Zones.**—Pathologists draw a sharp distinction between different zones within a hepatic lobule. Thus the central area, capillaries, and cells form the **hepatic vein zone**, which is specially liable to cyanotic changes; the area next the periphery of the lobule is the **portal vein zone**, whose cells under certain circumstances are particularly apt to undergo fatty degeneration; while there is an area lying midway between the two foregoing—the **hepatic artery zone**—which is specially liable to amyloid or waxy degeneration.]

3. **The liver cells** (fig. 227, II, *a*) are irregular polygonal cells of about $\frac{1}{1000}$ th of an inch (34 to 45 μ) in diameter (fig. 229). The arrangement of the capillaries

within a lobule determines the arrangement of the liver-cells. The liver-cells form anastomosing columns which radiate from the centre to the periphery of each lobule (figs. 228, 230).

[The liver-cells are usually stated to be devoid of an envelope, although Haycraft states that they possess one. They usually contain a single nucleus, with one or more nucleoli, but sometimes two nuclei occur. The protoplasm and nucleus of each cell contain a plexus of fibrils just like other epithelial cells. In some animals, globules

of oil and pigment-granules are found in the cell-protoplasm (fig. 229). Each cell is in relation with the wide-meshed blood-capillaries (fig. 227, *d, d*), and also with the much narrower meshwork of bile-ducts (*I, x*).

Changes in Liver-Cells.—The appearance of the cells varies with the **period of digestion**. During **hunger**, the liver-cells are finely granular and very cloudy (fig. 230), [and contain little glycogen, but many pigment-granules, and the nucleus is more frequently absent. Often free nucleoli and pale nuclei are found (*Ellenberger and Baum*). During **activity**, *i.e.*, after a full meal, especially of starchy food, the cells are larger and more distinct, stain more deeply with eosin, and contain fewer granules.] The protoplasm contains coarse, glancing hyaline



Fig. 228.

A liver lobule stained with picro-carmin (*Stirling*). BD., bile-duct; PV. and HV., portal and hepatic veins; HA., hepatic artery.

masses of glycogen (fig. 233, 2), and near the surface of the cell it is condensed, and a fine network stretches toward the centre of the cell, and in it is suspended the nucleus. All the hepatic cells are not in the same phase of activity at the same time. [Afanassiew finds that if the formation of bile in the liver be increased (*e.g.*, by section of the hepatic nerves, or feeding with proteids), the cells are moderately enlarged in size, and contain numerous granules, which are proteid in their nature; such cells resist the action of caustic potash. When there is a great formation of glycogen (as after feeding with potatoes and sugar), all the

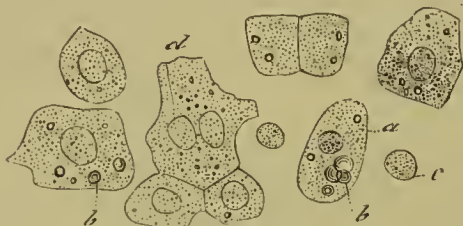


Fig. 229.

Human liver-cells containing oil-globules, *b* ;
a, has two nuclei.

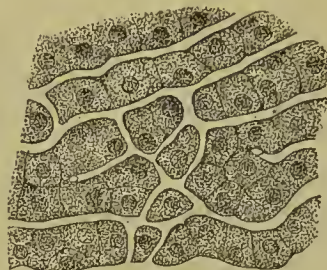


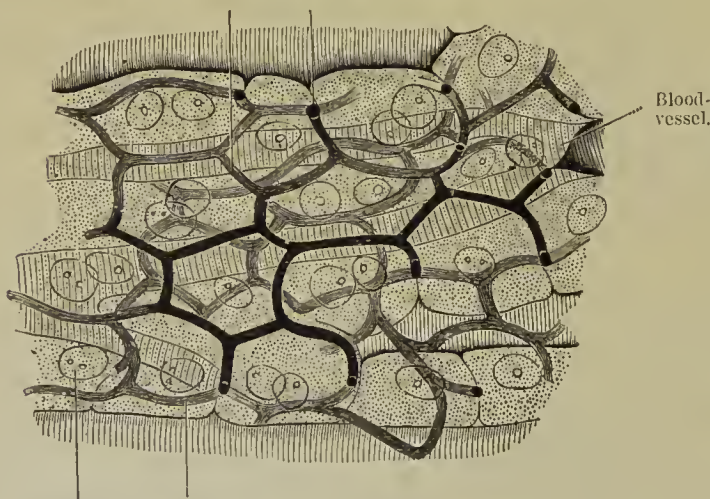
Fig. 230.

Liver-cells after withholding food for
36 hours.

cells are very large and sharply defined, and contain many granules of glycogen, the cells being so large as to compress the capillaries.]

[A. In frogs the appearance of the liver-cells varies with the season of the year. During the period from December to May—best studied in April—the cells are small, the nuclei large; and the cells contain very little or no glycogen. In the period from June to November—best studied in November—the cells are large, and contain many granules which are stained by eosin and nigrosin. They contain much glycogen (most in December), and their nuclei are small.]

Finest bile-capillary. Finest bile-capillary divided.



Nucleus of a liver-cell. Finest
bile-capillary.

Fig. 231.

Blood-capillaries; finest bile-capillaries or canaliculi in their
relative position in a rabbit's liver.

[The cells of a winter frog's liver contain in their protoplasm (1) hyaline granules of glycogen, usually arranged towards the outer part of the cell near the blood-vessel; (2) scattered throughout the protoplasm of the cell there may be fine granules of fat or oil; and, (3) small granules of a proteid nature, at the inner part of the cell next the bile capillary. The last-named granules diminish during digestion, and new ones appear to be formed in the intervals of digestion, so that there is an analogy between the liver-cells in this respect and other glands, *e.g.*, pancreas. All these substances may be recognised either directly or

by reagents; the glycogen gives a port-wine colour with iodine, and the fat is blackened by osmic acid, while the proteid granules are not affected by osmic acid, but disappear in caustic potash. If the glycogen be dissolved out by water the outer part of the cell-protoplasm appears vacuolated. If a frog be fed on carbohydrates the cells enlarge, and there is a great accumulation of glycogen in the cell, especially at its outer part, so as to compress the protoplasm. The port-wine reaction is very marked. In a summer frog, or a starved one, the cells are very

small and devoid of glycogen. In one fed on proteids there is little or no glycogen, and the cells are smaller and very granular.]

[**B. Mammals.**—Much the same changes occur; but in one fed on carbo-hydrates the glycogen accumulates in the protoplasm around the nucleus, and spreads out towards the periphery, leaving a compressed crust of protoplasm outside it. If the glycogen be dissolved out, wide vacuoles bounded by threads of protoplasm are seen in the cells. In the starved mammal the cells generally are like those of the frog under similar conditions.]

[**Action of Drugs on the Liver-Cells.**—Some substances excite the cells to activity, and cause them to present the appearance of cells in activity, *e.g.*, pilocarpin, muscarin, aloes; less so salicylate and benzoate of soda and rhubarb, while atropin and lead acetate inhibit the signs of activity. These results were obtained in the horse by Ellenberger and Baum. [Stolnikow, by using the quadruple-staining method of Ganle, finds that the hepatic cells of the frog undergo remarkable changes in poisoning by phosphorus. It is well known that this drug produces fatty degeneration of the liver-cells, but a deeper study shows that the changes are



Fig. 232.

Liver-cells of frogs. *a*, early, and *b*, late stage in poisoning by phosphorus; *c*, liver-cell of frog getting water only; *d*, getting sugar; and *e*, peptone (*Stirling after Stolnikow*).

both histological and chemical. Besides producing remarkable changes in the protoplasm of the cell, the protoplasm of the nucleus, in the form of small masses called plasmosoma, passes out into the cell-body, perhaps to renew the latter. The cells are increased in size, both after poisoning with phosphorus and after exision of the fat bodies in the frog (fig. 232). The fat present in the liver in phosphorus-poisoning is not present as droplets of oil, but probably in a loose combination, *e.g.*, lecithin, and as a matter of fact the amount of liver-lecithin is extraordinarily increased. There is also an increase of the nuelein; while glycogen is absent (*A. Leonard*). **Antipyrin** also produces profound changes, especially in the nuclei.]

4. The Bile-Ducts.—The finest bile-capillaries, channels, or canaliculi arise at the centre of the lobule, and indeed throughout the whole lobule they form a regular anastomosing network of very fine tubes or channels. Each cell is surrounded by a polygonal—usually hexagonal—mesh (figs. 233, 3, 234). The bile-capillaries always lie in the middle of the surface between two adjoining cells (fig. 227 II, *a*), where they form actual **intercellular passages** (fig. 231). [According to some observers, they are merely excessively narrow channels (1 to 2 μ wide) in the cement substance between the cells, while according to others they have a distinct delicate wall. The bile-capillary network is much closer than the blood-capillary network. Thus, there are *three* networks within each lobule—



Fig. 233.

1, Liver-cell, during fasting; 2, containing masses of glycogen; 3, a liver-cell surrounded with bile-channels, from which fine twigs proceed into the cell-substance to end in vacuoles.

- (1) A network of blood-capillaries;
- (2) " liver-cells;
- (3) " bile-capillaries; (fig. 231).

[The intralobular bile capillaries in man lie between two cells, but in the frog the channels lie at the junction of several hepatic cells, a fact best seen where the bile-capillary is cut transversely.]

Excessively minute **intracellular passages** are said to pass from the bile-capillaries into the interior of the liver-cells, where they communicate with certain small cavities or **vacuoles** (*Asp, Kupffer*) (fig. 233, 3). As the blood-capillaries run along the edge of the liver-cells, and the bile-capillaries between

the opposed surfaces of adjacent cells, the two systems of canals within the lobule are kept separate. Some bile-capillaries run along the edges of the liver-cells in the human liver, especially during embryonic life. Towards the peripheral part of the lobule, the bile-capillaries are larger, while adjoining channels anastomose, and leave the lobule, where they become **interlobular ducts** (fig. 227 *g*), which join with other similar ducts to form larger interlobular bile-ducts. These accompany the

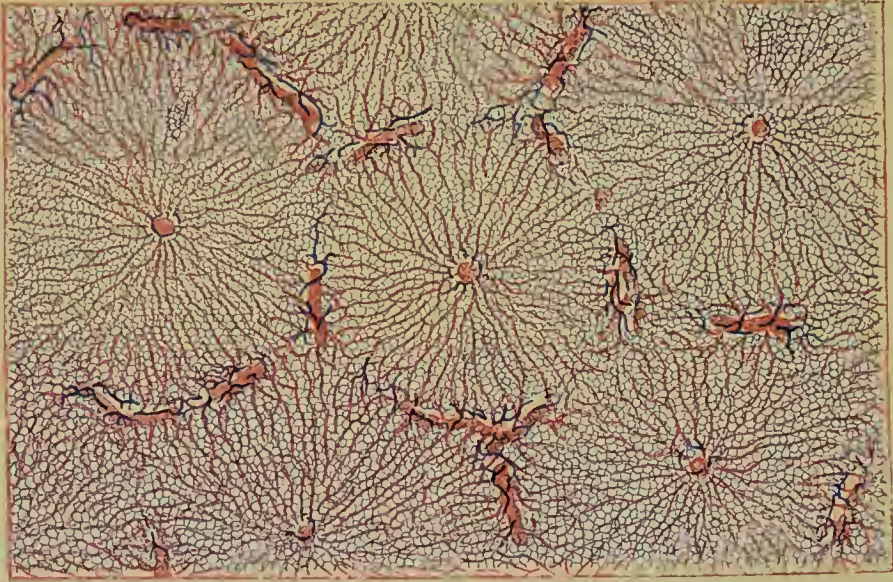


Fig. 234.

Blood-vessels of rabbit's liver injected with carmine (red). The bile-ducts and intralobular bile-capillaries are blue, being filled with a natural injection of sulph-indigotate of soda.

hepatic artery and portal vein, and leave the liver at the transverse fissure. The *finer* interlobular ducts, unlike ducts generally, frequently anastomose in Glisson's capsule, possess a structureless basement membrane, and are lined by a single layer of low polyhedral epithelial cells. The *larger* interlobular ducts have a distinct wall, consisting of connective and elastic tissue, mixed with circularly-disposed smooth muscular fibres (fig. 235). Capillaries are supplied to the wall, which is lined by a single layer of columnar epithelium. A sub-mucosa occurs only in the largest bile-ducts and in the gall-bladder. Smooth muscular fibres, arranged in single bundles, occur in the largest ducts, and as longitudinal and circular layers in the gall-bladder, whose mucous membrane is provided with numerous folds and depressions. The mucous membrane of the gall-bladder is pitted and the mucous membrane lining it. The epithelium lining it is cylindrical, with a distinct clear disc, and between these cells are tubular **mucous glands** occur in the larger bile-ducts and in the gall-bladder.

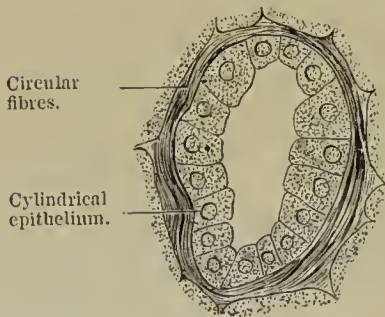


Fig. 235.

Interlobular bile-duct (human).

Vasa aberrantia are isolated bile-ducts which occur on the surface of the liver, but have no relation to any system of liver-lobules. They occur at the sharp margin of the liver, in the region of the inferior vena cava, of the gall-bladder, and of the parts near the portal fissure. It seems that the liver-lobules to which they originally belonged have atrophied and disappeared (*Zuckerkanll and Toldt*).

5. The lymphatics begin as *pericapillary* tubes around the capillaries within the lobules, emerge from the lobule, and run *within* the wall of the branches of the hepatic and portal veins, and afterwards surround the venous trunks, thus forming the *interlobular* lymphatics. These unite to form larger trunks, which leave the liver partly at the portal fissure, partly along with the hepatic veins, and partly at different points on the surface of the organ. There is a narrow superficial meshwork of lymphatics under the peritoneum—*sub-peritoneal*—which communicate with the thoracic lymphatics through the triangular ligament and suspensorium, while on the under surface they communicate with the lymphatics of the interlobular connective tissue.

6. The nerves consist partly of medullated but chiefly of non-medullated fibres from branches of the sympathetic, the terminal branches of the right vagus, and some branches of the left vagus to the hepatic plexus, the hepatic plexus being that part of the solar plexus which embraces the portal vein, bile-duct, and hepatic artery, as these pass into the liver at the portal fissure. They accompany the branches of the hepatic artery, and *ganglia* occur on their branches within the liver. Some of the nerve-fibres are vaso-motor in function, and, according to Pflüger, other nerve-fibres terminate directly in connection with liver-cells. [MacCallum describes an interlobular plexus of non-medullated fibres in man and Menobranchus, from which a perivascular and intercellular plexus proceeds. From the latter, fibrils pass to terminate within the cells near the nucleus.]

Pathological.—The connective tissue between the lobules may undergo great increase in amount, especially in alcohol and gin drinkers, and thus the substance of the lobules may be greatly compressed, owing to the cicatricial contraction of the newly-formed connective tissue (cirrhosis of the liver). In such interlobular connective-tissue, newly-formed bile-ducts are found.

Ligature of the ductus choledochus [causes enlargement of the spleen (rabbit), and a diminution in the number of the blood-corpuscles], and, after a time, interstitial inflammation of the liver. In rabbits and guinea-pigs the liver parenchyma disappears, and its place is taken by newly-formed connective tissue and bile-ducts (*Charcot and Gombault*). In all these cases of interstitial inflammation, there is proliferation of the epithelium of the bile-ducts.

[Regeneration of the Liver.—Tizzoni finds that there may be partial regeneration and new formation of liver-lobules in the dog, the process being the same as that which occurs in the embryonic development of the organ, *i.e.*, the growth of solid cylinders of liver-cells, formed by the pre-existing liver-cells, which penetrate into the connective tissue uniting the edges of the wound. These cells ultimately differentiate into hepatic cells and bile-ducts. Other observers attribute the new formation to outgrowths of the epithelial cells of the bile-cells.]

[Excision of Part of Liver.—Nearly three-fourths of a rabbit's liver may be excised, and still the animal may live in apparent health for months or even a year. This is due to the enormous regeneration of liver-tissue which takes place. Nearly the whole bulk of the organ removed may be reproduced, even if three-quarters of the liver be removed (*Ponfick*).]

174. CHEMICAL COMPOSITION OF THE LIVER-CELLS.—(1) **Proteids.**—The fresh, soft, parenchyma of the liver is *alkaline* in reaction; after death, coagulation occurs, the cell-contents appear turbid, the tissue becomes friable, and gradually an acid reaction is developed. This process closely resembles what occurs in muscle, and is due to the coagulation of a myosin-like body, which is soluble during life, but after death undergoes spontaneous coagulation (*Plósz*). The liver contains other proteids; **globulins** coagulating at 45°, 56°, and at 70° C., and mere traces of a cell-albumin coagulating at 70°–73° C. Nucleo-albumins appear to be absent (*Halliburton*). The nuclei contain nuclein. The connective-tissue yields gelatin.

(2) **Glycogen or Animal Starch.**—1.2 to 2.6 per cent.—is a true carbohydrate most closely related to inulin, apparently soluble in cold water, but perhaps only swelling up in water yielding an opalescent solution, which diffuses with difficulty. It has the formula $6(C_6H_{10}O_5) + H_2O$ [and may be regarded as a colloid-carbohydrate.] It is stored up in the liver-cells in amorphous granules around the nuclei (fig. 233, 2), and is uniformly distributed in all parts of the liver. Like inulin, it gives a deep red or *port-wine* colour with solution of iodine in iodide of potassium. It is changed into dextrin and sugar by diastatic ferments, and when

boiled with dilute mineral acids it yields grape-sugar (§ 148, I.; § 170, I.; § 252, III.). [It appears to play the same part in animal metabolism that starch does in the metabolism of plants. It represents a store of the excess of carbohydrates stored up in the organism for future use.]

Preparation of Glycogen.—[Feed a rabbit on carrots or boiled rice, and kill it three or four hours thereafter. Remove the liver immediately after death, cut it into fine pieces, and place these in *boiling* water, and boil it for some time in order to obtain a watery extract of the liver. The boiling water destroys the ferment supposed to be present in the liver, which would transform the glycogen into grape-sugar. To the cold filtrate are added alternately dilute hydrochloric acid and potassio-mercuric iodide, which precipitate the proteids. Filter, when a clear **opalescent fluid**, containing the glycogen in solution, is obtained. The glycogen is precipitated from the filtrate, as a white amorphous powder, on adding an excess of 70 to 80 per cent. alcohol. The precipitate is washed with 60 per cent. and afterwards with 95 per cent. alcohol, then with ether, and lastly, with absolute alcohol; it is dried over sulphuric acid and weighed (*Brücke*). *Külz* modifies the method somewhat. After boiling the liver for half an hour, it is rubbed up with liquor potassæ (100 grm. liver, 4 grm. KHO). Evaporate on a water-bath until all is dissolved, which occurs in about 3 hours. After cooling, neutralise with HCl and precipitate the proteids as above. The glycogen is precipitated with 96 per cent. alcohol, *i.e.*, until the solution contains 60 per cent. of alcohol. *F. Eves* asserts that the *post-mortem* conversion of sugar in the liver is not attributable to a ferment action, and the rapid appearance of sugar in the liver after death is due to the specific metabolic activity of the dying cells (p. 319).]

Sources.—These have been variously stated by different observers to be the carbohydrates of the food (*Pavy*); glycerin, taurin, and glycin (the latter splitting into glycogen and urica), the proteids (*Cl. Bernard*); and gelatin (*Salomon*). If glycogen is derived from the albumins, it must be formed from a non-nitrogenous derivative thereof.

Rohmann found that the use of ammonia carbonate and asparagin or glycin, along with a carbohydrate diet, in rabbits considerably increased the formation of glycogen. The acid formed in excessive amount, observed by *Stadelmann* in diabetes, unites with the ammonia and diminishes considerably the formation of glycogen.

Effects of Food.—Rabbits, whose livers have been rendered free from glycogen by starvation, yield new glycogen from their livers when they are fed with cane-sugar, grape-sugar, maltose, or starch. Active muscular movements soon make the liver of dogs free from glycogen; exposure to cold diminishes its amount. Dextrin and grape-sugar occur in the dead liver, but, in addition, some glycogen is found for a considerable time after death in the liver and in the muscles.

[*Pflüger* regards the formation of glycogen from proteids as a synthetic process. The molecular group (CH_2), present both in albumin and the fatty acids, must be changed into CH.OH by oxidation. The cells which cause this formation can also make use of these groups CH.OH , where they find them already present, as in sugar and glycerin. In this way the formation of glycogen from molecules derived from various sources is analogous to the formation of fat from carbohydrates or from proteids (§ 241).]

If glycogen is injected into the blood, aëroodextrin appears in the urine, and also hæmoglobin, as glycogen dissolves red blood-corpuscles. Ligature of the bile-duct causes decrease of the glycogen in the liver.

Other Situations.—Glycogen is not confined to the liver-cells; it occurs during foetal life in all the tissues of the body of the embryo [including the embryonic skeleton], in young animals (*Kühne*), the placenta [in the epithelial cells between the foetal and maternal tissues] (*Bernard*). It occurs in large amount in the liver during intra-uterine life. In the adult it occurs in the testicle, in the muscles (*MacDonnell*, *O. Nasse*), in numerous pathological products, in inflamed lungs (*Kühne*), and also in the corresponding tissues of the lower animals. [It also occurs in the chorionic villi, in colourless blood-corpuscles, in fresh pus cells which still exhibit amoeboid movements, and in fact in all developing animal cells, with amoeboid movement; the outer root-sheath of a hair-follicle (*Neisser*); it is a never-failing constituent in cartilage, and in the muscles and liver of invertebrata, such as the oyster. There is none in the fresh brain of the dog or rabbit, but it is found in the brain in diabetic coma (*Abeles*).]

Modifying Conditions.—If to a diet of proteids there be added large quantities of starch, milk-, fruit-, or cane-sugar, or glycerin, the amount of glycogen in the liver is very greatly increased (to 12 per cent. in the fowl), with a purely albuminous diet there is less glycogen, while a purely fatty diet diminishes it enormously.

During hunger it may disappear entirely. The injection of sugar or glycerin into a mesenteric vein of a starving rabbit causes the liver, previously free from glycogen, to contain glycogen (*Nannyn*). [It rapidly disappears from the liver of a rabbit by the action of cold, *e.g.*, cold baths and cold air. It would seem, therefore, to be a source of heat. Glycerin increases it, and also prevents the *post-mortem* change of glycogen into grape-sugar.]

[**Effect of Drugs on Glycogen.**—Arsenic, phosphorus, and antimony destroy the glycogenic function of the liver, no glycogen being present in the liver in animals poisoned with these drugs, so that puncture of the floor of the fourth ventricle no longer causes glycosuria in them. In animals poisoned by strychnia or curare, it is greatly diminished, both in the liver and in the muscles. Sugar is always present in the urine in the latter case but not in the former.]

During life, in the intervals of digestion under normal conditions, the glycogen is slowly and gradually transformed into grape-sugar, and the latter passes into the hepatic vein. The normal amount of sugar in blood is 0.5 to 1 per 1000, although the blood of the hepatic vein contains somewhat more [.2–.28 per cent.]. A considerable amount is transformed into sugar only when there is a decided derangement of the hepatic circulation, and in these circumstances the blood of the hepatic vein contains more sugar. The glycogen undergoes this change very rapidly after death, so that a liver which has been dead for some time always contains more sugar and less glycogen, the grape-sugar formed corresponding to the glycogen which disappears.

[**Glycogeny or Glycogenic Function of the Liver.**—The formation of glycogen in the liver is intimately related to the **general metabolic phenomena** in the body. In 1848 Bernard found that a considerable quantity of a reducing sugar was obtainable from the liver *after death*. In 1857, however, he found that if a liver be taken out of the body of a well-fed animal immediately after death and analysed, it did not contain sugar, but from it he obtained the body glycogen, the explanation of his first observation being that the glycogen normally existing in the cells of the living liver was rapidly converted into sugar after death. Pavy also showed that if the liver be examined as quickly as possible after death it contained only glycogen, with occasionally traces of sugar.

An extract of a liver rapidly removed from a “well-fed” animal after death always presents an opalescent appearance, due to glycogen, and it gives all the reactions of glycogen. If, however, an extract be made of a liver that has been removed several hours previously, and especially if the liver has been kept in a warm place, a decoction of such a liver is always clear and contains no glycogen, but much sugar. The glycogen has after death by some action or other been converted into sugar; the agency, whatever it is, is destroyed by the temperature of boiling water. It was suggested that the conversion was due to the action of a diastatic ferment, but this is highly doubtful. Diastatic ferments, *e.g.*, ptyalin, when they act on glycogen, convert it into maltose. Now, the sugar which is formed in the liver *post-mortem* is glucose. More probably it is due to the action of the living protoplasm of the hepatic cell, a view confirmed by Dastre (p. 321).]

[The quantity of glycogen in the liver varies in different species of animals, even under the same conditions of feeding, &c. MacDonnell gives the following:—

	Ratio of weight of body to weight of liver.	Percentage of glycogen.
Dog, ...	30.1	4.5
Cat, ...	19.1	1.5
Rabbit, ...	35.1	3.7
Guinea-pig, ...	21.1	1.4
Rat, ...	26.1	2.5
Pigeon, ...	44.1	2.5]

[That the amount of glycogen present in the liver is very variable, and is especially dependent on the nature and amount of the food, has already been

stated. Prolonged **fasting** causes it to disappear from the liver entirely in dogs in fifteen or sixteen days, and in rabbits in five days. Feeding with **carbohydrates** causes the greatest accumulation of glycogen in the liver, or rather a mixed diet containing some proteids, but with a large excess of carbohydrates. If a dog or fox be starved until all glycogen disappears from its liver, and then be fed on flesh, *i.e.*, **proteids**, glycogen accumulates in the liver; but not to such an extent as occurs after feeding with carbohydrates. The glycogen in the liver cannot be accounted for by the small quantities of glycogen that are present in the flesh, for small quantities of glycogen are formed in the liver even on a diet of fibrin, or gelatin. It seems, therefore, that some glycogen may be formed from proteids, and we know that when proteids are split up under certain conditions they yield a nitrogenous body and a carbon-containing non-nitrogenous residue; the latter may probably be the source of the glycogen in this case. **Fats** are in no way concerned in the storing up of glycogen in the liver.]

[The storing up of glycogen is also influenced by the **season of the year** apart from the taking of food. This is the case in the **frog**. There is a considerable storage of glycogen in the liver of the frog in winter, even though no food has been taken for some months; while in summer the liver contains very little (p. 314). The storage and disappearance of glycogen in the frog's liver are ultimately dependent on temperature. If a winter frog be kept warm for some days, its hepatic glycogen rapidly disappears. From the above it would seem that glycogen may be formed independently of matters obtained from the alimentary canal. The material for its formation must have been furnished from some part of the frog other than the intestinal tract.]

[It is obvious that the liver in some way or other manufactures glycogen either from the carbohydrates or proteids or from both supplied to it. One theory suggests that the sugar carried by the portal vein to the liver is dehydrated or loses water and is converted into glycogen, which is stored up in the hepatic cells. This view receives a certain amount of confirmation from Bernard's experiment of injecting grape-sugar into the jugular vein, when the sugar was excreted in the urine. If, however, the sugar was slowly injected into a rectal vein, a tributary of the portal vein—*i.e.*, the sugar had to traverse the liver before it reached the general circulation—none of the sugar appeared in the urine; at the same time there was an increase of glycogen in the liver. If this be the true view, then the liver-cells form a great **storehouse for the carbohydrates** during digestion, while the liver regulates the amount of sugar in the blood. It is known that if the sugar in the blood rises above a certain percentage (more than 0.3 per cent., normal amount 0.05–0.15), that it is excreted by the urine. Considering, then, the rapid absorption of sugar from the intestine during digestion, it seems necessary that so much sugar should not be thrown continuously into the general circulation. The liver, on this theory, catches and secures the sugar, and stores it up as glycogen. The blood of the portal vein during digestion contains more sugar than the hepatic vein, but the hepatic vein in the intervals of digestion contains more sugar—about twice as much—than the portal vein. This has been ascertained for the hepatic vein by catheterisation of the hepatic vein. A long flexible catheter is introduced through the jugular vein into the superior vena cava, and thence into the inferior vena cava; and it is so arranged that the inferior cava can be occluded below the hepatic vein, and from the latter blood can be drawn off and analysed.]

[This increase of the sugar in the hepatic vein is interpreted to mean that in the intervals of digestion the liver slowly and steadily re-converts the glycogen into sugar, and discharges the latter into the hepatic vein, in this way supplying the needs of the economy for this substance, yet preventing the percentage of sugar in the blood rising so high that it would be excreted by the urine.]

[It has been suggested that the glycogen in the liver is a preliminary phase in the constructive metabolism of fat. There are no good grounds of support for this view.]

[**Muscle-glycogen.**—Next to the liver it occurs in largest amount in the muscles, and it disappears from some muscles, at least during starvation. Even admitting that it is diminished during the working of a muscle, a muscle remains contractile without glycogen (§ 294).]

The **diastatic ferment** in the liver is small in amount, and can be obtained from the extract of the liver-cells by the same means as are applicable for obtaining other similar ferments, such as ptyalin; it does not seem to be formed within the liver-cells, but only passes very rapidly from the blood into them. The ferment seems to be rapidly formed when the blood-stream undergoes considerable derangement. A similar ferment is formed when red blood-corpuscles are dissolved (*Tiegel*), and, as red blood-corpuscles are continually destroyed within the liver, there is one source from which the ferment may be formed, whereby minute quantities of sugar would be continually formed in the liver.

[Dastre, like Eves, was unable to find a diastatic ferment in the liver capable of converting glycogen into grape-sugar, nevertheless, he admits that glycogen is converted into glucose in the liver. This, he says, is due to the activity of the protoplasm of the living hepatic cells. He has found an invert ferment in the liver.]

According to Seegen, the blood of the **hepatic vein** contains twice as much sugar (0.23 per cent.) as that in the portal vein (0.119 per cent.); observations on dogs showed that the blood flowing through the liver gives up over 400 grms. sugar in 24 hrs. Hence, in carnivora, the greatest part of the C of the animal food must pass into sugar, so that the formation of sugar in the liver, and its decomposition in the blood, or in the organs traversed by the blood, must be a very important function of the metabolism. Seegen is also of opinion that the liver-glycogen takes no part in the formation of sugar in the liver.

[Blood when perfused through a freshly excised liver (or through the kidneys, lungs, or muscles,) gains lactic acid (*Gaglio*). Lactic acid seems to be a normal constituent of the liver; at least when arterial blood or serum is perfused through the liver, the outflowing fluid contains lactic acid (*Gaglio*).]

(3) **Fats**, in the form of highly refractive granules, occur in the liver-cells, as well as free in the bile-ducts; sometimes, when the food contains much fat (more abundant in drunkards and the phthisical), olein, palmitin, stearin, volatile fatty acids, and sarcolactic acid are found.

There are also found traces of cholesterin, minute quantities of urea, uric acid, and the little-known body **jecorin**, $C_{105}H_{186}N_5SP_3O_{46}$, discovered by Drechsel, contains S and P, and reduces alkaline solutions of copper like grape-sugar. Its function is unknown, but its reducing action must be borne in mind in connection with reducing substances in the liver. It is also found in the spleen, muscles, and blood (*Baldi*). The liver of birds contains a relatively large amount of **uric acid**, even 6 to 14 times as much as the blood (*v. Schröder*). Lencin (? guanin), sarkin, xanthin, cystin and tyrosin occur pathologically in certain diseases where marked chemical decompositions occur.

[**Fatty degeneration and Infiltration.**—Fatty granules are of common occurrence within the cells of the liver, constituting fatty infiltration, and when not too numerous do not seem to interfere greatly with the functions of the liver-cells. Fatty particles occur if too much fatty food be taken, and they are commonly found in the livers of stall-fed animals; the well-known *pâté-de-foie gras* is largely composed of the livers of geese, which have been fed on large amounts of farinaceous food, and which have been subjected to other unfavourable hygienic conditions. Fatty granules are recognised by their highly refractive appearance, by their solubility in ether, and by being blackened by osmic acid. Even in health fatty granules are frequently present in the hepatic cells, especially those near the portal vein. During lactation also the liver contains much fat. In fishes the liver always contains much oil, and there seems to be some relation between the activity of the respiratory organs and the size of the liver; at any rate in fishes, where the respiration is less active—and the same is the case in embryos—the liver is always large, while birds with very active respiration have small livers. If a dog be fed on oil its hepatic cells readily become fatty.]

(4) The **inorganic substances** in the human liver are—potassium, sodium, calcium, magnesium, iron, manganese, chlorine, and phosphoric, sulphuric, carbonic, and silicic acids; while copper, zinc, lead, mercury, and arsenic may be accidentally deposited in the hepatic tissue.

[**Tizzoni's Reaction for Iron.**—If a section of a liver (especially of a young animal) hardened in alcohol be treated with a solution of potassic ferrocyanide, and then with dilute hydrochloric

acid, as a general rule the preparation becomes blue, even to the naked eye; but failing that, one can usually see with the microscope granules of Prussian blue in the protoplasm of the cells, indicating the presence of free iron oxide.] [If, as is very probable, the bile pigments are derived from a derivative of hemoglobin, what becomes of the iron? There are numerous combinations of iron in the liver, some simple, *e.g.*, oxide and phosphate, and some more stable organic combinations, *e.g.*, combined with nuclein, as an iron-nuclein called *hepatin* (§ 247, V.)]

175. DIABETES MELLITUS AND GLYCOSURIA.—[Glycosuria is characterised by the presence of **grape-sugar** in the urine. According to Brücke a *trace* of sugar exists normally in urine, and when this amount is increased we have glycosuria. When the normal amount of grape-sugar in the blood is increased, grape-sugar appears in the urine. The blood normally contains 0·05–0·15 per cent. of sugar, that of diabetics 0·22–0·44 per cent. When the percentage of sugar is artificially increased to 0·3 per cent., sugar passes into the urine. In **diabetes mellitus**, grape-sugar also appears in the urine, but this is really a serious disease, involving the alteration of many tissues, and distinguished by profound disturbance of the whole metabolic activity, which leads to numerous pathological changes and often to death. The appearance of grape-sugar in urine does not necessarily mean that a person is suffering from this disease. The abnormal increase of sugar in the blood is the cause of the appearance of sugar in the urine. The increase of sugar in the blood in diabetics seems to be due to the diminution in the amount of sugar decomposed.]

Temporary Glycosuria.—The formation of large quantities of grape-sugar by the liver, and its passage into the blood, and from the blood into the urine, constitute glycosuria. Extirpation of the liver in frogs, or destruction of the hepatic cells, as by fatty degeneration from poisoning with phosphorus or arsenic, does not cause this condition. It occurs after the injury of a certain part—the centre for the hepatic vaso-motor nerves, “diabetic centre”—of the *floor of the lower part of the fourth ventricle* at the level of the origin of the vagi (*Cl. Bernard's* “*piqûre*”). [The animal must be well fed previously, and the urine in a few hours will not only be increased in quantity, but contain sugar. The amount of sugar reaches a maximum and then declines; the urine becomes non-saccharine in a day or two, so that the glycosuria is only temporary. In a starved animal the urine will contain little or no grape-sugar. Glycosuria also occurs after section of the vagi, so that the vagi are not the channels through which the influences are conveyed to the liver to *excite* glycosuria. The *piqûre* is effective even after section of the vagi.] It also occurs after section of the vaso-motor channels in the spinal cord, from above down, as far as the exit of the nerves for the liver, *viz.*, to the lumbar region, and in the frog to the fourth vertebra (*Schiff*). When the vaso-motor nerves, which proceed from this centre to the liver, are cut or paralysed in any part of their course, mellituria or glycosuria is produced. All the nerve-channels do not run through the spinal cord alone. A number of vaso-motor nerves leave the spinal cord higher up, pass into the sympathetic, and thus reach the liver; so that destruction of the superior (*Pavy*), as well as of the inferior cervical sympathetic ganglion, and the first thoracic ganglion (*Eckhard*), the abdominal ganglia, and often of the splanchnic itself, produces it. The paralysis of the blood-vessels causes the liver to contain much blood, and the intrahepatic blood-stream is slowed. The disturbance of the circulation causes a great accumulation of sugar in the liver, as the blood-ferment has time to act upon the glycogen and transform it into sugar. By stimulation of the sympathetic at the lowest cervical and first thoracic ganglion, the hepatic vessels at the periphery of the liver-lobules become contracted and pale (*Cyon*). It is remarkable that glycosuria when present may be set aside by section of the splanchnic nerves. This is explained by supposing that the enormous dilatation and congestion, or the hyperæmia of the abdominal blood-vessels thereby produced, renders the liver anæmic. The vascularity of the liver produced by the

injury to the fourth ventricle may be due, not to paralysis of vaso-constrictor nerves, but to stimulation of vaso-dilator fibres. This, however, has not been proved.

[As to the **path of the nervous impulses** from the medulla oblongata to the liver there is great uncertainty. As already stated, they do not pass through the vagi. They certainly pass down the cervical spinal cord, then leave the cord to pass into the sympathetic. Cyon stated that they enter the lowest cervical ganglion, and pass through the annulus of Vieussens to the first dorsal ganglion and then through the sympathetic to the cœliac plexus, and by the hepatic plexus to the liver. As we have seen, section of certain of these nerves produces diabetes, but section of the splanchnic nerve does not always do so, although it gives rise to vaso-motor paralysis of the hepatic vessels. It is to be remembered, however, that section of the splanchnics paralyses the abdominal blood-vessels, and it may be that the great amount of vaso-motor paralysis thereby produced interferes with the velocity of the blood-stream through the liver. It is also to be remembered that the vaso-motor theory of glycosuria is by no means proved. The supposition that the nerves act directly on the hepatic cell protoplasm is by no means excluded.]

[**Reflex Production of Glycosuria.**—Continued stimulation of peripheral nerves may act reflexly upon the centre for the vaso-motor nerves of the liver. Diabetes has been observed to occur after stimulation of the central end of the vagus (*Cl. Bernard*), and also after stimulation of the central end of the depressor nerve (*Filshie*). [Neuritis of the vagus, produced by injection of ipecacuanha or croton oil, into the nerve trunk or by the action of a ligature is followed by glycosuria, which may last with intermissions for a month (*Arthaud and Butte*).] Even section and subsequent stimulation of the central end of the sciatic nerve causes diabetes. This may explain the occurrence of diabetes in people who suffer from sciatica. [It may occur also after perverted nervous activity, as psychical excitement, neuralgias (sciatica, trigeminal or occipital), concussion of the brain, as well as after certain injuries to the skull and vertebral column and some cerebral diseases.]

Other Causes of Glycosuria.—According to Schiff, the stagnation of blood in other vascular regions of the body may cause the ferment to accumulate in the blood to such an extent that diabetes occurs. The glycosuria that occurs after compression of the aorta or portal vein may perhaps be ascribed to this cause, but perhaps the pressure caused by these procedures may paralyse certain nerves. According to Eckhard, injury to the vermiform process of the cerebellum of the rabbit causes diabetes, [and so does injury to the cerebral peduncles and pons Varolii]. In man, affections of the above-named nervous regions cause diabetes. [Complete extirpation of the pancreas in dogs causes glycosuria (*v. Mering*).]

[In most individuals the use of a large quantity of sugar in the food is not followed by the appearance of sugar in the urine; but in some exceptional cases it is often present, *e.g.*, in persons suffering from gastric catarrh, especially if they are gouty.]

A number of **poisons** which paralyse the hepatic vaso-motor nerves produce diabetes; curare, CO, amyl nitrite, ortho-nitro-propionic acid, and methyl-delphinin [phloridzin (*v. Mering*)]; less certainly morphia, chloral hydrate, HCN, and some other drugs; and some infectious diseases. But congestion of the liver produced in other ways appears to cause diabetes, *e.g.*, after mechanical stimulation of the liver. To this class belongs the injection of dilute saline solutions into the blood (*Bock Hoffmann*), whereby either change in form or the solution of the coloured blood-corpuscles causes the congestion. The circumstance that repeated blood-letting makes the blood richer in sugar may perhaps be explained by the slowing of the circulation.

[**Curare-poisoning** causes glycosuria. This is not due to the artificial respiration necessary to keep curarised animals alive. It also occurs in frogs, and in these animals aeration of the blood can take place without the respiratory movements. Phloridzin is a glucoside, and it might be argued that the sugar formed under its influence was derived from the phloridzin itself, but the same effect is produced by phloretin, which is not a glucoside.]

[**Phloridzin-glycosuria.**—Most of the means which produce glycosuria in other animals fail to do so in birds; even the piqûre rarely produces it. This Thiel and Minkowski attribute to the intensely active oxidation-processes in birds. Phloridzin, a glucoside found in the root cortex of apple and cherry trees, causes glycosuria, even after extirpation of the liver, which shows that in these cases there are other causes at work than obtain in the other forms of glycosuria. Phloridzin makes animals, which are free from carbohydrates, diabetic. In this case the sugar must be derived from proteids (*v. Mering*). Phloridzin makes dogs diabetic within a few hours, but after two or three days the glycosuria disappears, but then the liver and muscles are free from glycogen. The administration of more phloridzin causes still more sugar to be excreted. This must proceed from proteid.]

Theoretical.—In order to explain the more immediate cause of these phenomena several hypotheses have been advanced:—

(a) The liver-glycogen may be transformed unhindered into sugar, as the blood in its passage through the liver deposits or gives up the ferment to the liver-cells. So that the normal function of the vaso-motor system of the liver, and its centre in the floor of the fourth ventricle, may be regarded as, in a certain sense, an "inhibitory system" for the formation of sugar.

(b) If we assume that normally there is continually a small quantity of sugar passing from the liver into the hepatic vein, we might explain the diabetes as due to the disappearance of those decompositions—diminished burning-up of the sugar in the blood, which are constantly removing the sugar from the blood. In fact, diabetic persons have been found to consume less O and to have an increased formation of urea.

Persons suffering from diabetes require a large amount of food; they suffer greatly from thirst, and drink much fluid. They exhibit signs of marked emaciation, when the loss of the body is greater than the supply. [In advanced diabetes the glycogenic function of the liver is almost abolished, as was proved by removing with a trocar a small part of the liver from man, when almost no glycogen was found (*Ehrlich*). The absorbed sugar in the portal vein passes directly into the general circulation without being submitted to the action of the liver (*v. Frerichs*).] In severe cases, towards death, not unfrequently a peculiar comatose condition—**diabetic coma**—occurs, when the breath often has the odour of **aceton**, which is also found in the urine. But neither aceton nor its precursor, aceto-acetic acid, nor æthyl-diacetic acid, nor the unknown substance, in diabetic urine, which gives the red colour with ferric chloride (*v. Jaksch*), is the cause of the coma (*Frerichs and Brieger*).

[**Injection of Grape-Sugar into the Blood.**—When grape-sugar is injected into the jugular vein of a dog, only 33 per cent. at most is given off in the urine; within 2 to 5 hours the urine is free from sugar. Even within a few minutes after the injection, only a certain proportion ($\frac{1}{2}$ – $\frac{1}{4}$) of the sugar is found in the blood; part of the sugar has been detected in the muscles, liver, and kidneys, but the fate of the remainder is not known. Immediately after the injection, the amount of hæmoglobin and also of serum-albumin is diminished (50 per cent.), which is due to increase of the quantity of water within the vessels; but within two hours the normal state is restored (*Brasol*). In a curarised dog the injection of grape-sugar into a vein increases the blood-pressure, but this effect is not observed after the injection of morphia and chloral.]

176. THE FUNCTIONS OF THE LIVER.—[To understand the functions of the liver, we must remember its **unique relation to the vascular and digestive systems**, whereby many of the products of gastric and intestinal digestion have to traverse it before they reach the blood, and some of them as they traverse the liver are altered. We have still much to learn regarding the liver. It has several distinct functions—some obvious, others not. (1) The liver **secretes bile**, which is formed by the hepatic cells, and leaves the organ by the bile-ducts, to pass into the duodenum. (2) The liver-cells also **form glycogen**, which does not pass into the ducts, but in some altered and diffusible form passes into the blood-stream, and leaves the liver by the hepatic veins. Hence, the study of the liver materially influences our conception of a secreting organ. In this case, we have the products of its secretory activity leaving it by two different channels—the one by the ducts, and the other by the blood-stream. The liver, therefore, is a great storehouse of carbohydrates, and it serves them out to the economy as they are required. It prevents the blood from being overwhelmed with sugar, and on the other hand it prevents a deficiency of this important body in the blood (*Bunge*). All this points to the liver as being an organ intimately related to the **general metabolism** of the body. (3) In a certain period of development it is concerned in the formation of blood-corpuscles (§ 7). (4) It has some relation to the breaking up of **blood-corpuscles** and the formation of **urea** and other metabolic products (§ 20, § 177, 3). (5) Some importance is attributed to the liver in connection with the arrest of certain substances absorbed from the alimentary canal, whereby they are either destroyed, stored up in the liver, or, it may be, prevented from entering the general circulation in too large amount. It is possible that ptomaines may be arrested in this way (§ 166). [It converts the poisonous aromatic products of putrefaction, *e.g.*, phenol, derived from proteids in the intestine, into harmless compounds by conjugation with sulphates (§ 262).]

[The liver has no special action on certain mineral substances which traverse it in the blood, *e.g.*, potassic chloride, but it retains the vegetable alkaloids, provided they are not present in

too large an amount in the blood. The ptomaines are similarly retained in the liver. The liver is said to possess this property only as long as it contains glycogen (*H. Rogers*).]

[Heger, in his experiments on the artificial circulation of blood through an excised liver, found that blood to which an alkaloid (nicotin) was added, after being perfused through the liver lost some of its nicotin. Again, a dose of nicotin or hyoseyamine that proves fatal when injected subcutaneously, does not do so when it is injected into a branch of the portal vein (*Schiff and Lautenbach*).]

177. CONSTITUENTS OF THE BILE.—[The bile, although it is secreted continuously, and passes along the hepatic duct in most animals, is only poured into the intestine at certain times. In the intervals it is carried along the cystic duct and stored up in the gall-bladder. At certain times it is poured out by the common bile-duct into the duodenum.]

[Bile is a yellowish-brown or dark-green coloured transparent fluid, with a sweetish, strongly bitter taste, feeble musk-like odour, and neutral reaction. The specific gravity of human bile from the gall-bladder = 1026 to 1032, while that from a fistula = 1020 to 1011. It contains no proteids.]

The following table gives its composition in different animals—

100 parts Bile of—	Man.	Ox.	Pig.	Dog. Gall-bladder.	Fresh Secreted.
Water, ...	86.3	90.4	88.8	85.2	95.3
Solids, ...	13.7	9.6	11.2	14.8	4.7
Bile, salts, leecithin, } cholesterin, fats, } soaps, ... }	8.2 } 2.5 }	8.0 }	7.3 }	12.6 }	3.4 }
Mucus and pigment,	2.2	0.3	0.6	0.3	0.2
Inorganic salts, .	0.8	1.3	1.1	0.6	0.6

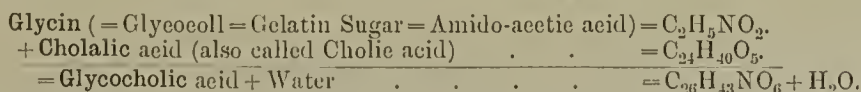
It contains—

(1) **Mucus**, which gives bile its sticky character, and not unfrequently makes it alkaline: it is the product of the mucous glands and the goblet-cells of the mucous membrane of the larger bile-duets. When bile is exposed to the air, the mucus causes it to putrefy rapidly. It is precipitated by acetic acid, or alcohol.

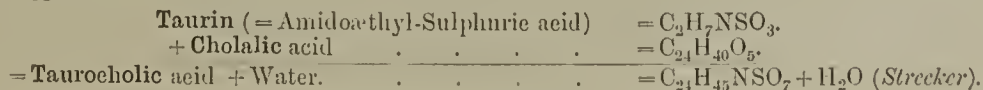
[The bile formed in the ultimate bile-duets does not seem to contain mucus or mucus, but bile from the gall-bladder always does, the difference in composition of bile from the gall-bladder and bile from the liver-duct being shown in the above table. The bile in the gall-bladder is more concentrated, so that absorption of water occurs in the gall-bladder. The mucus is partly formed by the mucous glands in the larger bile-duets, and partly by the cells lining the gall-bladder (§ 173). It is not a true mucus, but rather a nucleo-albumin.]

(2) **The Bile-Acids.**—**Glycocholic** and **taurocholic acids**, so-called conjugate-acids, are united with soda (in traces with potash) to form glycocholate and taurocholate of soda, which have a bitter taste, and rotate the plane of polarised light to the right. In human bile (as well as in that of birds, many mammals, and amphibians) taurocholic acid is most abundant; in other animals (pig, ox) glycocholic acid is most abundant but is absent in sucklings.

(a) **Glycocholic acid**, $C_{23}H_{43}NO_6$, when boiled with caustic potash, or baryta water, or with dilute mineral acids, takes up H_2O and splits into—



(b) **Taurocholic acid**, $C_{26}H_{45}NSO_7$, when similarly treated, takes up water and splits into—



[Solutions of taurocholic acid are antiseptic, and if sufficiently strong interfere with the development of bacteria, and prevent the alcoholic and lactic fermentations, as well as the tryptic and diastatic action of the pancreas (*Emick*).]

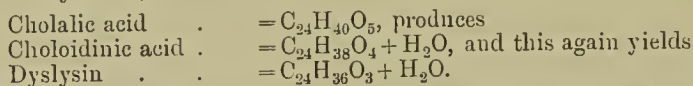
Preparation of the Bile-Acids.—Evaporate bile to $\frac{1}{4}$ of its volume, rub it up into a paste with excess of animal charcoal, and dry at 100° C. Extract the black mass with absolute alcohol, and filter. After a part of the alcohol has been removed by distillation, the bile-salts are precipitated in a resinous form, and on the addition of excess of ether, there is formed immediately a crystalline mass of glancing needles (Plattner's "crystallised bile"). The alkaline salts of the bile-acids are freely soluble in water or alcohol, and insoluble in ether. Neutral lead acetate precipitates the glycocholic acid—as lead glycocholate—from the solution of both salts; the precipitate is collected on a filter, dissolved in hot alcohol, and the lead is precipitated as lead sulphide by H_2S ; after removal of the lead sulphide, the addition of water precipitates the isolated glycocholic acid. If, after precipitating the lead glycocholate, the filtrate be treated with *basic* lead acetate, a precipitate of lead taurocholate is formed, from which the acid may be obtained in the same way as described above (*Strecker*).

With regard to the **decomposition products** of the bile-acids, **glycin**, as such, does not occur in the body, but only in the bile in combination with cholic acid, in urine in combination with benzoic acid, as hippuric acid, and lastly, in gelatin in complex combination. [The constitution of glycin is known. It is the same as amido-acetic acid $\text{CH}_2(\text{NH}_2)\text{COOH}$. In the body it originates from proteid (*Bunge*).]

Cholalic acid rotates the ray of polarised light to the right, and its chemical constitution is unknown. It is insoluble in water, soluble in alcohol, but soluble with difficulty in ether, from which it separates in prisms. Its crystalline alkaline salts are readily soluble in water. It is coloured blue by iodine, and occurs free only in the intestine.

Cholalic acid is replaced in the bile of many animals by a nearly related acid, *e.g.*, in pig's bile, by hyo-cholalic acid (*Strecker*); in the bile of the goose, cheno-cholalic acid is present (*Marsson, Otto*). [Cholalic acid obtained from the bile-acids of various animals differs in its composition. The formula of cholalic acid from human bile is $\text{C}_{18}\text{H}_{38}\text{O}_4$, while that from ox bile is $\text{C}_{24}\text{H}_{40}\text{O}_5$.]

When cholalic acid is boiled with concentrated HCl , or heated dry at 200° C., it becomes an anhydride, thus:—



Choloidinic acid is, however, not improbably a mixture of cholalic acid and dyslysin; dyslysin, when fused with caustic potash, is changed into cholalate of potash. By oxidation cholalic acid yields a tribasic acid, as yet uninvestigated, and a fair amount of oxalic acid, but no fatty acids (*Clève*).

[**Taurin** is derived from proteids, as shown by its composition and by the sulphur it contains.]

Pettenkofer's Test.—The bile-acids, cholic acid, and their anhydrides, when dissolved in water, yield on the addition of $\frac{2}{3}$ concentrated sulphuric acid (added in drops so as not to heat the fluid above 70° C.), and several drops of a 10 per cent. solution of cane-sugar, a *reddish-purple* transparent fluid, which shows two absorption-bands at E and F (*Schenk*). [A very good method is to mix a few drops of the cane-sugar solution with the bile, and to shake the mixture until a copious froth is obtained. Pour the sulphuric acid down the side of the test-tube, and then the characteristic colour is seen in the froth. Any albumin present must be removed before applying the test.]

According to Drechsel, it is better to add phosphoric acid, instead of sulphuric acid, until the fluid is syrupy, then add the cane-sugar, and afterwards place the whole in boiling water. When investigating the amount of bile-acids in a liquid, the albumin must be removed beforehand, as it gives a reaction similar to the bile-acids, but in that case the red fluid has only *one* absorption-band. If only small quantities of bile-acids are present, the fluid must in the first place be concentrated by evaporation. Pettenkofer's test depends on the formation of furfural from the sugar and H_2SO_4 , furfural giving a red with the bile-acids (*Mylius*). In place of sugar a 1 per cent. watery solution of furfural may be used.

[**Hay's Test.**—The bile-acids or their soluble salts *lower the surface-tension of fluids* in which

they are dissolved. Throw a small quantity of sulphur (sublimed or precipitated) on the surface of the fluid containing bile-acids, and if the bile-acids be present, the sulphur will at once begin to sink, and will be wholly precipitated within a few minutes. (*Privately communicated.*)

The bile-acids are formed in the liver. After its extirpation, there is no accumulation of biliary matters in the blood.

How the formation of the nitrogenous bile-acids is effected is quite unknown. They must be obtained from the decomposition of albuminous materials, and it is important to note that the amount of bile-acids is increased by albuminous food. Taurin contains part of the sulphur of albumin; bile-salts contain 4 to 4.6 per cent., which may perhaps be derived from dissolved red blood-corpuscles.

(3) **The Bile-Pigments.**—The freshly secreted bile of man and many animals has a yellowish-brown colour, due to the presence of **bilirubin**. [In cases of human biliary fistula Robson found that in fresh human bile the pigment is biliverdin.] When it remains for a considerable time in the gall-bladder, or when alkaline bile is exposed to the air, the bilirubin absorbs O, and becomes changed into a green pigment, **biliverdin**. This substance is present naturally, and is the chief pigment in the bile of herbivora and cold-blooded animals. [Both pigments behave like acids; they form soluble compounds with the potassium group, and insoluble ones with the calcium group (*Bunge*). The actual amount of colouring matter in bile is always very small.]

Anthen finds that living hepatic cells when brought into contact with a solution of hæmoglobin outside the body take up hæmoglobin, and (glycogen being present in them) convert it into a pigment closely related to the bile-pigment.

The bile-pigments are:—

(a) **Bilirubin** ($C_{32}H_{36}N_4O_6$) is perhaps united with an alkali; it crystallises in transparent fox-red clinorhombic prisms. It is insoluble in water, *soluble in chloroform*, by which substance it may be separated from biliverdin, which is insoluble in chloroform. It unites as a monobasic acid with alkalies, and as such is soluble. It is identical with Virehow's hæmatoidin (§ 20).

Preparation.—It is most easily prepared from the red (bilirubin-chalk) gall-stones of man or the ox. The stones are pounded, and their chalk dissolved by hydrochloric acid; the pigment is then extracted with chloroform. That bilirubin is derived from hæmoglobin is very probable, considering its identity with hæmatoidin. Very probably red blood-corpuscles are dissolved in the liver, and their hæmoglobin changed into bilirubin.

(b) **Biliverdin** ($C_{32}H_{36}N_4O_8$) is an oxidised derivative of the former, from which it can be obtained by various oxidation-processes. It is readily *soluble in alcohol*, very slightly so in ether, and not at all soluble in chloroform. It occurs in the placenta of the bitch. As yet it has not been retransformed by reducing agents into bilirubin.

Tests for Bile-Pigments.—Bilirubin and biliverdin may occur in other fluids, e.g., the urine, and are detected by the **Gmelin-Heintz' reaction**. When *nitric acid containing some nitrous acid* is added to a liquid containing these pigments, a play of colours is obtained, beginning with *green* (biliverdin), blue—violet—red, ending with yellow. [This reaction is best done by placing a drop of the liquid on a *white* porcelain plate, and adding a drop of the *impure* nitric acid.]

(c) If, when the blue colour is reached, the oxidation process is arrested, **bilicyanin** (*Heynsius, Campbell*), in acid solution blue (in alkaline violet), is obtained, which shows two ill-defined absorption-bands near D (*Jaffé*).

(d) **Bilifuscin** occurs in small amount in decomposing bile and in gall-stones = bilirubin + H_2O .

(e) **Biliprasin** (*Stüdtler*) also occurs = bilirubin + H_2 + O.

(f) The yellow pigment, which ultimately results from the prolonged action of the oxidising reagent, is the **choletelin** ($C_{16}H_{18}N_2O_6$) of Maly; it is amorphous, and soluble in water, alcohol, acids, and alkalies.

[Spectrum of Bile.]—The bile of carnivorous animals is generally free from absorption-bands, except when acids are added to it, in which case the band of bilirubin is revealed. Bilirubin and biliverdin yield characteristic spectra only when they are treated with nitric acid. The

bile of some animals yields bands, but when this is the case they are due to the presence of a derivative of hæmatin, and MacMunn calls this body **cholo-hæmatin**, which gives a three- or four-banded spectrum (ox, sheep).]

(g) Bilirubin absorbs $H + H_2O$ (by putrefaction, or by the treatment of alkaline watery solutions with the powerfully reducing sodium amalgam), and becomes converted into Maly's **hydrobilirubin** ($C_{32}H_{40}N_4O_7$), which is slightly soluble in water, and more easily soluble in solutions of salts, or alkalies, alcohol, ether, chloroform, and shows an absorption-band at *b*, F. This substance, which, according to Hammarsten, occurs in normal bile, is a constant colouring-matter of fæces, and was called **stercobilin** by Vaulair and Masius, but is identical with hydrobilirubin (*Maly*). It is, however, probably identical with the urinary pigment *urobilin* of Jaffé (*Stokvis*, § 20).

[According to MacMunn, hydro-bilirubin differs from urobilin. There is a close resemblance between pathological bilirubin and stercobilin. The bile of **invertebrates** contains none of the bile-pigments present in vertebrates, although hæmochromogen is found in the cray-fish and pulmonate molluscs. In some organs, and in bile, a pigment-like vegetable chlorophyll—**entero-chlorophyll**—is found, but whether it is derived from without, or formed within the organism, is not certain (*MacMunn*).]

[**Electrolysis of bile.**—When ox-bile is electrolysed in a U-tube, oxidation of the pigment takes place at the positive electrode, bilirubin being changed into biliverdin, and with a strong or long-continued current the biliverdin may in its turn give place to higher oxidation products. Reversal of the current will now cause the process to retrace its steps, and the bile-pigment will pass through bilirubin to a more reduced stage where the colour is yellow (*Haycraft and Scofield*). The spectrum of the bile, however, remains practically unchanged amidst the play of oxidation and reduction. The substance which causes the absorption bands does not therefore belong to the bilirubin series. The changes produced in the pigment by electrolysis are not due to the direct action of the current, but to the action of the products set free at the electrodes. The bile-salts, on the other hand, are electrolytes (*G. N. Stewart*).]

(4) **Cholesterin**, $C_{26}H_{44}O + H_2O$, is a monatomic alcohol which rotates the ray of polarised light to the left; it occurs also in blood, yolk, nervous matter [and gall-stones]. It forms transparent rhombic plates, which usually have a small oblong piece cut out of the corner (fig. 236). It is insoluble in water, soluble in hot alcohol, ether, or chloroform. It is kept in solution in the bile by the bile-salts. [The quantity is considerable. It may reach 2 per cent.]

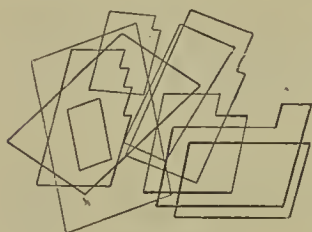


Fig. 236.

Crystals of cholesterin.

Preparation.—It is most easily prepared from so-called white gall-stones, which not unfrequently consist entirely of cholesterin, by extracting them with hot alcohol after they are pulverised. Crystals are excreted after evaporation of the alcohol. **Tests.**—They give a red colour with sulphuric acid (5 vol. to 1 vol. H_2O), while they give a blue—as cellulose does—with sulphuric acid and iodine. When dissolved in chloroform, one drop of concentrated sulphuric acid causes a deep red colour (*H. Schiff*). Moistened with an alcoholic solution of alcohol, on adding H_2SO_4 , the crystals exhibit a green, blue, and red colouration. Dissolved in glacial acetic acid, H_2SO_4 =red, and then a blue colour (*Liebermann*).

(5) Amongst the other organic constituents:—**Lecithin** (§ 23), or its decomposition-product, neurin (cholin), and glycerophosphoric acid (into which lecithin may be artificially transformed by boiling with baryta); **palmitin**, **stearin**, **olein**, as well as their soda **soaps**; **diastatic ferment**; traces of **urea**; (in ox-bile, acetic acid and propionic acid, united with glycerin, and metals, *Dogiel*).

(6) **Inorganic constituents of bile** (0.6 to 1 per cent):—

They are—sodic and potassic chloride, calcic and magnesic phosphate, and much iron, which in fresh bile gives the ordinary reactions for iron, so that iron must occur in one of its oxidised compounds in bile; manganese and silica. **Gases.**—Freshly-secreted bile contains in the dog more than 50 vol., and in the rabbit 109 vol. per cent. CO_2 , partly united to alkalies, partly absorbed, the latter, however, being almost completely absorbed within the gall-bladder.

The mean composition of human bile is :—

Water, . . .	82 to 90 per cent.	Lecithin, . . .	0·5 per cent.
Bile-salts, . . .	6 to 11 „	Mucin and pigments, 1 to 3 „	
Fats and soaps, . . .	2 „	Ash, . . .	0·61 „
Cholesterin, . . .	0·4 „		

Further, unchanged fat probably always passes into the bile, but it is again absorbed therefrom (*Virchow*). The amount of S in dry dog's bile = 2·8 to 3·1 per cent., the N = 7 to 10 per cent. (*Spiro*); the sulphur of the bile is not oxidised into sulphuric acid, but it appears as a sulphur-compound in the urine (*Kunkel, v. Voit*). In birds deprived of their liver there is no formation of bile.

[**Comparative.**—Dog's bile is bright yellow and contains taurocholate only; cat's bile has the same composition whatever the nature of the food. The bile of the fox and wolf contains traces of glycocholate. In herbivora the bile is generally green in colour and contains both glycocholate and taurocholate of soda, but that of the sheep contains only traces of the former. Pig's bile is turbid, reddish-brown, filters easily, and contains two special biliary acids—hyoglycocholic and hyotaurocholic. In the guinea-pig it is like amber in colour and becomes green on exposure to the air. Bird's bile is generally green, and so is that of the frog; the latter contains taurocholic acid. In fishes the bile contains chiefly taurocholic acid. *Amphioxus* has no bile. The so-called biliary secretion of the invertebrates does not seem to be true bile (*Beaunis*).]

178. SECRETION OF BILE.—(1) The secretion of bile is not a mere filtration of substances already existing in the blood of the liver, but it is a chemical production of the characteristic biliary constituents, accompanied by oxidation, within the hepatic cells, to which the blood of the gland only supplies the raw material. The liver-cells themselves undergo histological changes during the process of digestion. It is secreted continually; but part is stored up in the gall-bladder, and is poured out copiously during digestion. The higher temperature of the blood of the hepatic vein, as well as the large amount of CO₂ in the bile, indicates that oxidations occur within the liver. The water of the bile is not merely filtered through the blood-capillaries, as the pressure within the bile-ducts [15–17 mm. Hg.] may exceed that in the portal vein [7 mm. Hg.]

[Liver cells while still alive can produce bile salts from a mixture of hæmoglobin and glycogen, a process which is favoured by the addition of soda or serum (*Kallmeyer and Alex. Schmidt*).]

(2) The quantity of bile was estimated by v. Wittich, from a biliary fistula, at 533 cubic centimetres in twenty-four hours (some bile passed into the intestine); by Westphalen, at 453 to 566 grms. [by Murchison, at 40 oz.]; by Joh. Ranke, on a biliary-pulmonary fistula, at 652 cubic centimetres; Copeman and Winston, 700–800 c.c. The observation by Ranke gives 14 grms. (with 0·44 gm. solids) per kilo. of man in twenty-four hours. The mean is 1290 c.c. per day in a man weighing 70 kilos. [Mayo Robson found in cases of biliary fistula an average of 30 oz. More is secreted during the day than at night.]

Analogous values for **animals** are—1 kilo. dog, 32 grms. (1·2 solids); 1 kilo. rabbit, 137 grms. (2·5 solids); 1 kilo. guinea-pig, 176 grms. (5·2 solids).

(3) The excretion of bile into the intestine shows two maxima *during one period of digestion*; the first from 3 to 5 hours, and the second from 13 to 15 hours, after food. This seems to be due to simultaneous reflex excitement of the hepatic blood-vessels, which become greatly dilated.

(4) The influence of food is very marked. The largest amount is secreted after a flesh diet, with some fat added, less after vegetable food; a very small amount with a pure fat diet; it stops during hunger. [Mayo Robson did not find it to be materially influenced by diet.] Draughts of water increase the amount, with a corresponding relative diminution of the solid constituents. [The biliary solids are increased by food, reaching their maximum about one hour after feeding.]

(5) The influence of blood-supply is variable :—

(a) Secretion is greatly favoured by a copious and rapid blood-supply. The blood-pressure is not the prime factor, as ligature of the cava above the diaphragm, whereby the greatest blood-pressure occurs in the liver, *arrests* the secretion. [It would seem, as in the case of the kidney, that the velocity of the blood has far more to do with it than the blood-pressure.]

(b) Simultaneous ligature of the hepatic artery (diameter $5\frac{1}{2}$ mm.) and the portal vein (diameter, 16 mm.) abolishes the secretion (*Röhrig*). These two vessels supply the raw material for the secretion of bile.

(c) If the hepatic artery be ligatured, the portal vein alone sustains the secretion. Ligature of the artery or of one of its branches ultimately causes necrosis of the parts supplied by that branch, and eventually of the entire liver, as this artery is the nutrient vessel of the liver.

(d) If the branch of the portal vein to one lobe be ligatured, there is only a slight secretion in that lobe, so that the bile must be formed from the arterial blood. Complete ligature of the portal vein rapidly causes death (§ 87). Neither ligature of the hepatic artery by itself, nor *gradual* obliteration of the portal vein by itself, causes cessation of the secretion, but it is diminished. That *sudden* ligature of the portal vein causes cessation is due to the fact that, in addition to diminution of the secretion, the enormous stagnation of blood in the rootlets of the portal vein in the abdominal organs makes the liver very anæmic, and thus prevents it from secreting.

(e) If the blood of the hepatic artery is allowed to pass into the portal vein (which has been ligatured on the peripheral side), secretion continues (*Schiff*).

(f) Profuse loss of blood arrests the secretion of bile, before the muscular and nervous apparatus become paralysed. A more copious supply of blood to other organs—*e.g.*, to the muscles of the trunk—during vigorous exercise, diminishes the secretion, while the transfusion of large quantities of blood increases it, but if too high a pressure is caused in the portal vein, by introducing blood from the carotid of another animal, it is diminished.

(g) **Influence of Nerves.**—All conditions which cause contraction of the abdominal blood-vessels, *e.g.*, stimulation of the ansa Vieusseuii, of the inferior cervical ganglion, of the hepatic nerves, of the splanchnics, of the spinal cord (either directly by strychnia, or reflexly through stimulation of sensory nerves), affect the secretion; and so do all conditions which cause stagnation or congestion of the blood in the hepatic vessels (section of the splanchnic nerves, diabetic puncture, § 175), section of the cervical spinal cord. Paralysis (ligature) of the hepatic nerves causes *at first* an increase of the biliary secretion. [Stimulation of the nerves around the hepatic artery causes at first an acceleration, and afterwards slowing of the secretion. Section of these nerves causes a decided acceleration. Doubtless these results are due to variations in the calibre of the vessels and bile-ducts.]

(h) **Portal and Hepatic Veins.**—With regard to the raw material supplied to the liver by its blood-vessels, it is important to note the difference in the composition of the blood of the hepatic and portal veins. The blood of the hepatic vein contains *more* sugar, lecithin, cholesterolin (?), (*Drosdoff*), and blood-corpuscles, but *less* albumin, fibrin, hæmoglobin, fat, water, and salts.]

(i) Uffelmann observed that the flow of bile from a person with a biliary fistula was arrested during fever.]

(6) The formation of bile is largely dependent upon the decomposition of red blood-corpuscles, as they supply the material necessary for the formation of some of its constituents.

Hence, all conditions which cause solution of the coloured blood-corpuscles are accompanied by an increased formation of bile (§ 180).

[The specific constituents of bile.—The bile-acids and pigments are formed in the liver. (1) These substances do not exist in the general blood-stream. (2) In frogs, after removal of the liver, these substances are not found in the blood. (3) After ligature of the bile-ducts, and all the vessels passing to the liver in pigeons, the biliary secretion is arrested, but even after twenty-four hours none of the specific biliary constituents were found in the tissues or blood. No bile pigments were found in the blood-serum (*Stern*). Had the bile constituents been formed outside the liver, they would have accumulated in the blood and tissues. After ligature of the bile-ducts only in pigeons, biliary pigment is found in the blood and urine. The same is true of biliary acids as proved by Fleischl (p. 332).]

[As to the sources of the specific biliary constituents, the glycocol and taurin of the bile-acids, containing as they do nitrogen, must be derived from a proteid molecule, but cholic acid—an acid free from N—does not necessarily arise from proteids.]

[That the bile-pigments are formed from hæmoglobin resulting from the breaking up of hæmoglobin is believed from the following considerations:—(1) In old apoplectic clots—hæmatoidin—a body nearly identical with bilirubin is found (§ 20). There is a genetic relation between bile-pigments and hæmatin :—

Hæmatin, $C_{32}H_{32}N_4O_4Fe$.

Bilirubin, $C_{32}H_{36}N_4O_6$.

Biliverdin, $C_{32}H_{36}N_4O_8$.

(2) Substances which cause solution of the blood-corpuscles within the vascular system increase the quantity of bile-pigments, *e.g.*, the intra-venous injection of water, bile-salts, hæmoglobin. (3) Moreover, the bile contains iron in the form of a phosphate, and the iron is perhaps obtained from the iron of the decomposed Hb. (4) Bile-pigments are only found in the vertebrata,—that is, in those animals whose blood contains hæmoglobin. They do not occur in invertebrata. *Amphioxus*, which has no red blood-corpuscles, forms no bile-pigments.]

(7) Of course a normal condition of the hepatic cells is required for a normal secretion of bile.

[(8) **Age.**—The age of the individual does not appear to influence greatly its composition nor does sex influence it.]

Biliary Fistulæ.—The mechanism of the biliary secretion is studied in animals by means of biliary fistulæ. Schwann made a **permanent biliary fistula**. He opened the belly by a vertical incision a little to the right of the ensiform process, cut into the fundus of the gall-bladder, and sewed its margins to the edges of the wound in the abdomen, and afterwards introduced a cannula into the wound (fig. 237). To secure that all the bile is discharged externally, tie the common bile-duct in two places and divide it between the two ligatures. After a fistula is freshly made the secretion falls. This depends upon the removal of the bile from the body. If bile be supplied, the secretion is increased. Regeneration of the divided bile-duct may occur in dogs. V. Wittich observed a biliary fistula in man. [A **temporary biliary fistula** may also be made. The abdomen is opened in the same way as described above. A long bent glass cannula is introduced and tied into the common bile-duct, and the cystic duct is ligatured or clamped (fig. 237). The tube is brought out through the wound in the abdomen.]

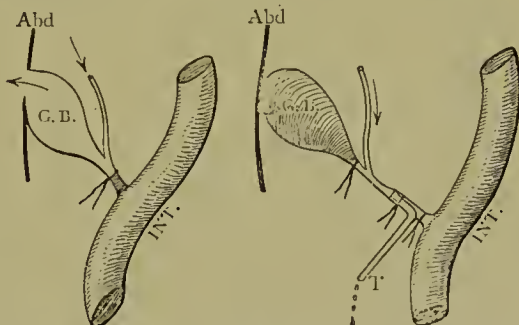


Fig. 237.

Schwann's permanent fistula, and a temporary fistula. *Abd.*, abdominal wall; *G.B.*, gall-bladder; *INT.*, intestine; *T.*, tube in temporary fistula (*Stirling*).

[Influence of the Liver on Metabolism.]—If the liver be excluded from the circulation, important changes must necessarily occur in the metabolism. In **birds** (goose) there is an anastomosis between the portal system of the liver and that of the kidneys, so that, when the portal circulation is interrupted in these animals, there is never any great congestion in the abdominal organs. The goose dies generally eight to ten hours after the operation. The *uric acid* in the urine rapidly falls to a minimum ($\frac{1}{30}$ to $\frac{1}{40}$ of normal); the chief constituent of the urine is then sarcolactic acid, while in normal urine there is none; the ammonia is increased (*Minkowski*). This experiment goes to indicate that uric acid is formed in the liver. **Dog.**—If the liver be excluded from the portal circulation, by connecting the portal vein with the inferior vena cava, and ligaturing the hepatic artery, a dog will live in the former case three to six days, and in the latter one to two. The liver does not undergo necrosis, nor does bile cease to be secreted. The liver is nourished by the blood in the hepatic vein, the reflux in this vein being probably caused by the respiratory movements (*Stolnikow*). Noël Paton finds that in dogs, in a condition of nitrogenous equilibrium, some drugs which increase the flow of bile (*e.g.*, salicylate and benzoate of soda, colchicum, perchloride of mercury, and euonymin) also increase the production of urea; hence, he concludes that the formation of urea in the liver bears a very direct relationship to the secretion of bile (§ 256).]

179. EXCRETION OF BILE.—[In this connection we must keep in view two distinct mechanisms. (1) The **bile-secreting mechanism** dependent upon

the liver-cells, which are always in a greater or less degree of activity ; (2) the **bile-expelling mechanism**, which is specially active at certain periods of digestion (§ 178).]

Excretion of bile is due to (1) the continual pressure of the newly-formed bile within the interlobular bile-duets forcing onward the bile in the excretory duets.

(2) The interrupted **periodic compression of the liver** from above, by the diaphragm, at every inspiration. Further, every inspiration assists the flow of blood in the hepatic veins, and every respiratory increase of pressure within the abdomen favours the current in the portal vein.

It is probable that the diminution of the secretion of bile, which occurs after bilateral division of the vagi, is to be explained in this way ; still it is to be remembered, that the vagus sends branches to the hepatic plexus. It is not decided whether the biliary excretion is diminished after section of the phrenic nerves and paralysis of the abdominal muscles.

(3) The *contraction of the smooth muscles* of the larger bile-duets and the gall-bladder. Stimulation of the spinal cord, from which the motor nerves for these structures pass, causes acceleration of the outflow, which is afterwards followed by a diminished outflow. Under normal conditions, this stimulation seems to occur reflexly, and is caused by the passage of the ingesta into the duodenum, which, at the same time, excite movement of this part of the intestine.

(4) Direct stimulation of the liver, and reflex stimulation of the spinal cord, diminish the excretion ; while extirpation of the hepatic plexus and injury to the floor of the fourth ventricle do not exert any disturbing influence.

(5) A relatively small amount of resistance causes bile to stagnate in the bile-duets.

Secretion Pressure.—A manometer, tied into the gall-bladder of a guinea-pig, supports a column of 200 millimetres of *water* or 15 mm. Hg ; and secretion can take place under this pressure. If this pressure be increased, or too long sustained, the watery bile passes from the liver into the blood, even to the amount of four times the weight of the liver, thus causing solution of the red blood-corpuscles by the absorbed bile ; and very soon thereafter hæmoglobin appears in the urine. [This fact is of practical importance, as duodenitis may give rise to symptoms of jaundice, the resistance of the inflamed mucous membrane being sufficient to arrest the outflow of bile.]

Passage of Substances into the Bile.—Some substances which enter the blood pass into the bile ; especially the metals, copper, arsenic, iron, &c. ; potassium iodide, bromide, and sulphocyanide, and turpentine [the latter gives it an odour of violets] ; to a less degree, cane-sugar and grape-sugar ; sodium salicylate, and carbolic acid. If a large amount of water be injected into the blood, the bile becomes albuminous ; mercuric and mercurous chlorides cause an increase of the water of the bile. Sugar has been found in the bile in diabetes ; leucin and tyrosin in typhus, lactic acid and albumin in other pathological conditions of this fluid.

180. REABSORPTION OF BILE ; JAUNDICE.—**I. Absorption-Jaundice.**—When resistance is offered to the outflow of bile into the intestine, *e.g.*, by a plug of mucus, or a gall-stone which occludes the bile-duct, or where a tumour or pressure from without makes it impervious—the bile-duets become filled with bile and cause an enlargement of the liver [and may give rise to obstructive, mechanical, or hepatogenous jaundice.] The pressure within the bile-duets is increased. As soon as the pressure has reached a certain amount, which it soon does when the bile-duct is occluded (in the dog 275 mm. of a column of bile), reabsorption of bile from the distended larger bile-duets takes place into the *lymphatics* (not the blood-vessels) of the liver, the bile-acids pass into the lymphatics of the liver. [The lymphatics can be seen at the portal fissure filled with yellow-coloured lymph.] The lymph passes into the thoracic duct, and so into the blood (*Fleischl*). Even when the pressure is very low within the portal vein, bile may pass into the blood without any obstruction to the bile-duct being present. This is the case in *Icterus neonatorum*, as after ligature of the umbilical cord no more blood passes through the umbilical vein ; further, in the *icterus of hunger*, “*hunger-jaundice*,” as the portal vein is relatively empty, owing to the feeble absorption from the intestinal canal (*Cl. Bernard*). [Jaundice is readily produced by inhalation of arsenicretted hydrogen or the administration of toluylendiamin.]

II. Cholæmia may also occur, owing to the excessive production of bile (*hypercholia*), the bile not being all excreted into the intestine, so that part of it is reabsorbed. This takes place when there is solution of a great number of blood-corpuscles (§ 178, 6), which yield material for the formation of bile. Thick inspissated bile accumulates in the bile-duets, so that stagnation,

with subsequent reabsorption of the bile, takes place. The transfusion of heterogeneous blood obtained by dissolving coloured blood-corpuscles acts in this direction. Icterus is a common phenomenon after too copious transfusion of the same blood. The blood-corpuscles are dissolved by the injection into the blood of heterogeneous blood-serum, by the injection of bile-acids into the vessels, and by other salts, by phosphoric acid, water, chloral, inhalation of chloroform and ether; the injection of dissolved hæmoglobin into the arteries or into a loop of the small intestine acts in the same way.

Icterus Neonatorum.—When, owing to compression of the placenta within the uterus, too much blood is forced into the blood-vessels of the newly-born infant, a part of the surplus blood during the first few days becomes dissolved, and part of the hæmoglobin is converted into bilirubin, thus causing jaundice (*Virchow, Violet*).

Absorption-Jaundice.—When the jaundice is caused by the absorption of bile already formed in the liver, it is called hepatogenic or absorption-jaundice. The following are the symptoms:—

(1) Bile-pigments and bile-acids pass into the tissues of the body; hence, the most pronounced external symptom is the yellowish tint or *jaundice*. The skin and the sclerotic become deeply coloured yellow. In pregnancy the fœtus is also tinged.

(2) Bile-pigments and bile-acids pass into the urine (not into the saliva, tears, or mucus), (§ 177). When there is much bile-pigment, the urine is coloured a deep yellowish-brown, and its froth is citron-yellow; while strips of gelatin or paper dipped into it also become coloured. Occasionally bilirubin (= hæmatoidin) crystals occur in the urine (§ 266).

(3) The *feces* are “*clay coloured*” (because the hydrobilirubin of the bile is absent from the faecal matter)—*very hard* (because the fluid of the bile does not pass into the intestine); contain much *fat* (in globules and crystals), because the fat is not sufficiently digested in the intestine without bile, so that 78 per cent. of the fat taken with the food reappears in the *feces* (*v. Voit*); they have a very *disagreeable odour*, perhaps because the bile normally limits the putrefaction in the intestine. [*V. Voit* finds that putrefaction does not take place if fats be withheld from the food (p. 335).] The *evacuation of the feces* occurs *slowly*, partly owing to the hardness of the *feces*, partly because of the absence of the peristaltic movements of the intestine, owing to the want of the stimulating action of the bile.

(4) The *heart-bets* are greatly diminished, *e.g.*, to 40 per minute. This is due to the action of the bile-salts, which at first stimulate the cardiac ganglia, and then weaken them. Bile-salts injected into the heart produce at first a temporary acceleration of the pulse, and afterwards slowing (*Röhrig*). The same occurs when they are injected into the blood, but in this case the stage of excitement is very short. The phenomenon is not affected by section of the vagi. It is probable, that when the action of the bile-salts is long continued, they act upon the heart-muscle. In addition to the action on the heart, there is slowing of the respiration and *diminution of temperature*.

(5) That the *nervous system*, and perhaps also the muscles, are affected, either by the bile-salts or by the accumulation of cholesterin in the blood, is shown by the very general relaxation, sensation of fatigue, weakness, drowsiness, and lastly deep coma—sometimes there is sleeplessness, itchiness of the skin, even mania, and spasms. Löwit, after injecting bile into animals, observed phenomena referable to stimulation of the respiratory, cardio-inhibitory, and vaso-motor nerve-centres.

(6) In very pronounced jaundice there may be “*yellow vision*,” owing to the impregnation of the retina and macula lutea with the bile-pigment.

(7) The bile-acids in the blood dissolve the red blood-corpuscles. The hæmoglobin is changed into new bile-pigment, and the globulin-like body of the hæmoglobin may form urinary cylinders or casts in the urinary tubules, which are ultimately washed out of the tubules by the urine.

Influence of Drugs on the Secretion of Bile.—On animals one may make either a permanent or a temporary fistula (p. 331). The latter is the more satisfactory method, and the experiments are usually made on fasting curarised dogs. A suitable cannula is introduced into the common bile-duct (fig. 237), the animal is curarised, artificial respiration being kept up, while the drug is injected into the stomach or intestine. Röhrig used this method, which was improved by Rutherford and Vignal. Röhrig found that some purgatives—croton oil, colocynth, jalap, aloes, rhubarb, senna, and other substances—increased the secretion of bile. Rutherford and Vignal investigated the action of a large number of drugs on the bile-secreting mechanism. They found that croton oil is a feeble hepatic stimulant, while podophyllin, aloes, colchicum, euonymin, iridin, sanguinarin, ipecacuan, colocynth, sodium phosphate, phytolaccin, sodium benzoate, sodium salicylate, dilute nitro-hydrochloric acid, ammonium phosphate, mercuric chloride (corrosive sublimate), are all powerful, or very considerable, hepatic stimulants. Some substances stimulate the intestinal glands, but not the liver, *e.g.*, magnesium sulphate, castor oil, gamboge, ammonium chloride, manganese sulphate, calomel. Other substances stimulate the liver as well as the intestinal glands, although not to the same extent, *e.g.*, scammony

(powerful intestinal, feeble hepatic stimulant); colocynth excites both powerfully; jalap, sodium sulphate, and baptisin, act with considerable power both on the liver and the intestinal glands. Calabar bean stimulates the liver, and the increased secretion caused thereby may be reduced by sulphate of atropin, although the latter drug, when given alone, does not notably affect the secretion of bile. The injection of water or bile slightly increases the secretion. In all cases where purgation was produced by purely intestinal stimulants, such as magnesium sulphate, gamboge, and castor oil, the secretion of bile was diminished. In all such experiments it is most important that the *temperature of the animal be kept up*, else the secretion of bile diminishes. Paschik's results on dogs differ considerably from those of Rutherford. He asserts that only the bile-acids (salts) of all the substances he investigated excite a prompt and distinct cholagogue action. Baldi also asserts that he has not observed a decided increase of the secretion following the use of some of the so-called cholagogues.]

[Biliary fistula sometimes occur in man. The bile-duct may be completely blocked by gall-stones. Sometimes the gall-bladder is opened to remove the gall-stones, and occasionally a biliary fistula persists, the bile being wholly discharged through an opening, none reaching the intestine owing to occlusion of the common bile-duct. In a case observed by Mayo Robson, he found that many so-called cholagogues, *e.g.*, euonymin, rhubarb, podophyllin, carbonate of soda, turpentine, benzoate of soda, seem rather to diminish than increase the amount of bile excreted; iridin appears to increase the flow temporarily without augmenting the total quantity in 24 hours.]

[As yet we cannot say definitely whether or not such substances as stimulate the secretion of bile do so by exciting the mucous membrane of the small intestine and thereby inducing reflex excitement of the liver. Their action does not seem to be due to increase of the blood-stream through the liver. More probably, as Rutherford suggests, these drugs act directly on the hepatic-cells or their nerves. Acetate of lead directly depresses the biliary secretion, while some substances affect it indirectly.]

[Cholesteræmia.—Flint ascribes great importance to the excretion of cholesterin by the bile, with reference to the metabolism of the nervous system. Cholesterin, which is a normal ingredient of nervous tissue, is excreted by the bile, and if it be retained in the blood "cholesteræmia," with grave nervous symptoms, is said to occur. This, however, is problematical, and the phenomena described are probably referable to the retention of the bile-acids in the blood.]

181. FUNCTIONS OF THE BILE.—[(1) Bile is concerned in the digestion of certain food-stuffs;

(2) Part is absorbed, a fact opposed to the view that bile is entirely an excretion.

(3) Part is excreted. Perhaps the bile is largely excrementitious; at least, observations in cases of biliary fistula in man have shown that increase in body-weight and good health are quite consistent with the entire absence of bile from the intestines (*M. Robson*).]

(A) Bile plays a part in the **absorption of fats**.—[The presence of bile in the intestine is not absolutely necessary for the digestion of such an amount of fat as is capable of supporting life and keeping up nutrition.]

(1) It *emulsifies neutral fats*, whereby the fatty granules pass more readily through or between the cylindrical epithelium of the small intestine into the lacteals. It does *not* decompose neutral fats into glycerin and a fatty acid, as the pancreas does (§ 170, III.).

When, however, fatty acids are dissolved in the bile, the bile-salts are decomposed, the bile-acids being set free, while the soda of the decomposed bile-salts readily forms a soluble soap with the fatty acids. These soaps are soluble in the bile, and increase considerably the emulsifying power of this fluid. Bile can dissolve fatty acids to form an acid fluid, which has high emulsifying properties (*Steiner*). Emulsification is influenced by a 1 per cent. solution of NaCl, or Na₂SO₄.

(2) As fluid fat flows more easily through capillary tubes moistened with bile, it is concluded that, when the pores of the wall of the small intestine are moistened with bile, the fatty particles pass more easily through them.

(3) Filtration of fat takes place through a membrane moistened with bile or bile-salts under less pressure than when it is moistened with water or salt solutions (*v. Wistinghausen*). [Gröper has repeated *v. Wistinghausen's* experiment, but with negative results.]

(4) As bile, like a solution of soap, has a certain relation to watery solutions, as

well as to fats, it permits diffusion to take place between these two fluids, as the membrane is moistened by both fluids.

Bile is of importance in the absorption of fats. This is strikingly illustrated by experiments on **animals**, in which the bile is entirely discharged externally through a fistula. Dogs under these conditions absorbed at most 40 per cent. of the fat taken with the food [60 per cent. being given off by the fæces, while a normal dog absorbs 99 per cent. of the fat]. The chyle of such animals is very poor in fat, is not white but transparent; the fæces, however, contain much fat, and are oily; the animals have a ravenous appetite; the tissues of the body contain little fat, even when the nutrition of the animals has not been much interfered with. Persons suffering from disturbances of the biliary secretion, or from liver affections, ought, therefore, to abstain from fatty food. [The digestion of flesh and gelatin is not interfered with in dogs by the removal of the bile (*v. Voit*). Dogs with biliary fistula can digest albumin and carbohydrates as completely as normal dogs. The putrefactive smell of the fæces in dogs with intestinal fistula is due to the unabsorbed fat enclosing the proteids, which become decomposed by the putrefactive organisms of the intestine (*Bunge*).]

(B) Fresh bile contains a **diastatic ferment**, which transforms starch into sugar, and also glycogen into sugar. [This is a very feeble diastatic action, and is apparently not greater than that possessed by some other non-digestive juices in the body. Bile has no action on albumin.]

(C) Bile excites **contractions of the muscular coats** of the intestine, and contributes thereby to absorption. [In cases of biliary fistula in man regular action of the bowels may occur without the presence of bile in the intestine.]

(1) The bile-acids act as a stimulus to the **muscles of the villi**, which contract from time to time, so that the contents of the origins of the lacteals are emptied towards the larger lymphatics, and the villi are thus in a position to absorb more. [The villi act like numerous small pumps, and expel their contents, which are prevented from returning by the presence of valves in the larger lymphatics.]

(2) The **musculature of the intestine** itself seems to be excited, perhaps through the agency of the plexus myentericus. In animals with a biliary fistula, and in which the bile-duct is obstructed, the intestinal peristalsis is greatly diminished, while the salts of the bile-acids administered by the mouth cause diarrhoea and vomiting. As contraction of the intestine aids absorption, bile is also necessary in this way for the absorption of the dissolved food-stuffs.

(D) The presence of bile seems to be necessary to the vital activity of the intestinal epithelium in its supposed function of being concerned in the absorption of fatty particles (§ 190).

(E) Bile moistens the wall of the intestines, and gives to the fæces their normal amount of water, so that they can be readily evacuated. Animals with a biliary fistula, and some individuals with obstruction of the bile-ducts, are very costive. The mucus aids the forward movement of the ingesta through the intestinal canal. Thus, in a certain sense, bile is a *natural purgative*.

(F) The bile diminishes putrefactive decomposition of the intestinal contents, especially with a fatty diet, § 190. [Thus, it is an **antiseptic**, although this is doubted by *v. Voit*. Its so-called antiseptic action is quite unimportant. Bile itself rapidly decomposes outside the body.]

(G) When the strongly acid contents of the stomach pass into the duodenum the glycocholic acid is precipitated by the gastric acid, and carries the pepsin with it (*Burkart*). Some of the albumin, which has been simply *dissolved* (but not peptone or propeptone), is also precipitated by the taurocholic acid (*Maly and Emich*). The bile-salts are decomposed by the acid of the gastric juice. When the mixture is rendered alkaline by the pancreatic juice and the alkali derived from the decomposition of the bile-salts, the pancreatic juice acts energetically in this alkaline medium (*Moleschott*).

[Taurocholic acid and its soda salts precipitate albumin, but not peptone; glycocholic acid does not precipitate albumin, so that in the intestine the peptone is separated from the albumin (and syntonin), and may therefore be more readily absorbed, while the precipitate adhering to the intestinal wall can be further digested (*Maly and Emich*). Taurocholic acid behaves in the same way towards gelatin peptone.]

Bilious Vomit.—When the bile passes into the stomach, as in vomiting, the acid of the gastric

juice unites with the bases of the bile-salts; sodium chloride and free bile-acids are formed, and the acid-reaction is thereby somewhat diminished. The bile-acids cannot carry on gastric digestion; the neutralisation also causes a precipitation of the pepsin and mucin. As soon, however, as the walls of the stomach secrete more acid, the pepsin is redissolved. The bile which passes into the stomach deranges gastric digestion, by shrivelling the proteids, which can only be peptonised when they are swollen up (p. 297).

182. FATE OF THE BILE.—Some of the biliary constituents are completely evacuated with the fæces, while others are reabsorbed by the intestinal walls. [A considerable proportion of the bile is excreted.]

(1) **Mucin** passes unchanged into the fæces.

(2) The **bile-pigments** are reduced, and are partly excreted with the fæces as **hydrobilirubin**, and partly as the identical end-product **urobilin** by the urine (§ 177, 3 g).

From **meconium** hydrobilirubin is absent, while crystalline bilirubin and biliverdin, and an unknown red oxidation-product of them, are present [bile-acids, even taurocholic, and small traces of fatty acids] (*Zweifel*), so that it gives Gmelin's reaction. Hence, no reduction—but rather oxidation—processes occur in the foetal intestine. [**Composition of meconium.**—Dary gives 72·7 per cent. water, 23·6 mucus and epithelium, 1 per cent. fat and cholesterin, and 3 per cent. bile-pigments. *Zweifel* gives 79·78 per cent. water, and solids 20·22 per cent. It does not contain lecithin, but so much bilirubin that Hoppe-Seyler uses it as a good source whence to obtain this pigment. It gives a spectrum of a body related to urobilin.]

(3) **Cholesterin** is given off with the fæces.

(4) The **bile-salts** are for the most part reabsorbed by the walls of the jejunum and ileum, to be re-employed in the animal's economy. Tappiner found them in the chyle of the thoracic duct—minute quantities pass normally from the blood into the urine. Only a very small amount of glycocholic acid appears unchanged in the fæces. The taurocholic acid, as far as it is not absorbed, is easily decomposed in the intestine, by the putrefactive processes, into cholalic acid and taurin; the former of these is found in the fæces, but the taurin at least seems not to be constantly present. Part of the cholalic acid is absorbed, and may unite in the liver either with glycin or taurin (*Weiss*).

(5) The fæces contain mere traces of **lecithin**.

Impaired Nutrition.—The greatest part of the most important biliary constituents, the bile-acids, re-enter the blood, and thus is explained why animals with a biliary fistula, where all the bile is removed (without the animal being allowed to lick the bile), rapidly lose weight. This depends partly upon the digestion of the fats being interfered with, and also upon the direct loss of the bile-salts. If such dogs are to maintain their weight, they must eat twice as much food. In such cases, carbohydrates most beneficially replace the fats. If the digestive apparatus is otherwise intact, the animals, on account of their voracity, may even increase in weight, but the flesh and not the fat is increased.

Bile partly an Excretion.—The fact that bile is secreted during the foetal period, whilst none of the other digestive fluids is, proves that it is an *excretion*.

The cholalic acid which is reabsorbed by the intestinal walls passes into the body, and seems ultimately to be burned to form CO_2 and H_2O . The **glycin** (with hippuric acid) forms urea, as the urea is increased after the injection of glycin. The fate of **taurin** is unknown. When large quantities are introduced into the human stomach, it reappears in the urine as tauro-carbamic acid, along with a small quantity of unchanged taurin. When injected subcutaneously into a rabbit, nearly all of it reappears in the urine.

[**Practical.**—In practice it is important to remember that bile, once in the intestine, is liable to be absorbed unless it be carried down the intestine; hence, it is one thing to give a drug which will excite the secretion of the bile, *i.e.*, a hepatic stimulant, and another to have the bile so secreted expelled. It is wise, therefore, to give a drug which will do both, or at least to combine a hepatic stimulant with one which will stimulate the musculature of the intestine as well. *Active exercise*, whereby the diaphragm is vigorously called into action to compress the liver, will aid in the expulsion of the bile from the liver (*Bruntton*).]

183. THE INTESTINAL JUICE.—**Length of Intestine.**—The human intestine is ten times longer than the length of the body, as measured from the vertex to the anus. It is longer comparatively than that of the omnivora. Its minimum length is 507, its maximum 1194 centimetres [17 to 35 feet]; its capacity is relatively greater in children (*Bencke*) (§ 159).

The **succus entericus** is the digestive fluid secreted by the numerous glands of the intestinal mucous membrane. The largest amount is produced by Lieberkühn's glands, while in the duodenum there is added the scanty secretion of Brunner's glands.

Brunner's glands are small, branched, tubular glands, lying in the sub-mucosa of the duodenum. Their fine ducts run inwards, pierce the mucous membrane, and open at the bases of the villi (figs. 214, 238). The acini are lined by cylindrical cells, like those lining the pyloric glands. In fact, Brunner's glands are structurally and anatomically identical with the pyloric glands of the stomach. During hunger, the cells are turbid and small, while during digestion they are large and clear. The glands receive nerve-fibres from Meissner's plexus (*Drasch*).

I. The Secretion of Brunner's Glands.

—The granular contents of the secretory cells of these glands, which occur singly in man, but form a continuous layer in the duodenum of the sheep, besides *proteids*, consist of *mucin* and a *ferment-substance* of unknown constitution. The watery extract of the glands causes—(1) Solution of proteids at the temperature of the body (*Krolow*). (2) It also has a diastatic action. It converts maltose into glucose (*Brown and Heron*). It does not appear to act upon fats.

On account of the smallness of these objects, such experiments are only made with great difficulty, and, therefore, there is a considerable uncertainty with regard to the action of the secretion.

Lieberkühn's glands are simple tubular glands resembling the finger of a glove [or a test-tube], which lie closely packed, vertically near each other, in the mucous membrane (fig. 239); they are most numerous in the large intestine, owing to the absence of villi in this region. They consist of a structureless *membrana propria* lined by a single layer of low cylindrical epithelium, between which numerous goblet-cells occur, the goblet-cells being fewer in the small intestine and much more numerous in the large (fig. 239). The glands of the small intestine yield a thin secretion, while those of the large intestine yield a large amount of sticky mucus from their goblet-cells (*Klose and Heidenhain*). [In a vertical section of the small intestine they lie at the base of the villi (figs. 238, 249). In transverse section they are shown in fig. 240.]

II. The Secretion of Lieberkühn's Glands, from the duodenum onwards, is the chief source of the intestinal juice.

Intestinal Fistula.—The intestinal juice is obtained by making a **Thiry's Fistula** (1864). A loop of the intestine of a dog is pulled forward (fig. 241), and a piece about 4 inches in length is cut out, so that the continuity of the intestinal tube is broken, but the mesentery and its blood-vessels are not divided. One end of this tube is closed, and the other end is left open and stitched to the abdominal wall (fig. 241, 3). The two ends of the intestine, from which this piece was taken, are brought together with sutures, so as to establish the continuity of the intestinal canal (fig. 241, 2). The excised pieces of intestine yield a secretion which is uncontaminated with any other digestive secretion. [Thiry's method is very unsatisfactory, as judged from the action of the separated loop in relation to medicaments, probably owing to its mucous membrane becoming atrophied from disuse, or injured by inflammation.]

[Meade Smith makes a small opening in the intestine, through which he introduces two

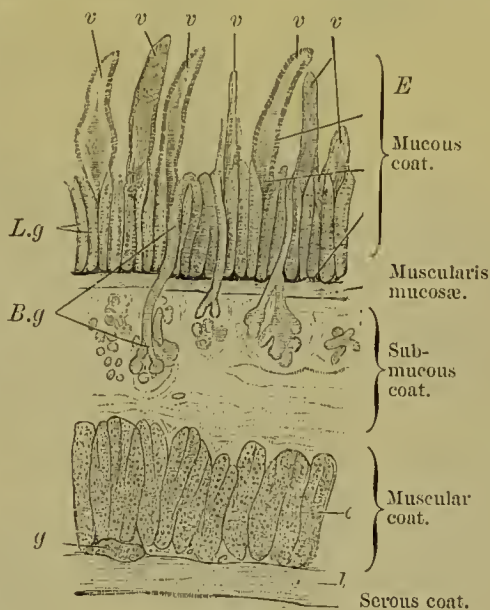


Fig. 238.

Vertical section of duodenum (cat) $\times 30$. *E*, epithelium; *c* and *l*, circular and longitudinal muscular fibres; *L.g.*, Lieberkühn's glands; *B.g.*, Brunner's glands; *g*, ganglion cells; *v*, villi.

small collapsed india-rubber balls, one above and the other below the opening, which are then distended by inflation until they completely block a certain length of the intestine. The loop thus blocked off, having been previously well washed out, is allowed to become filled with succus, which is secreted on the application of various stimuli. By means of Bernard's gastric cannula (§ 165) inserted into the fistula in the loop, the secretion can be removed when desired.]

[**Vella's Fistula.**—Open the belly of a dog, and pull out a loop (30 to 50 cm.) [1 to 1½ feet] of small intestine, and ligature it; divide it above and below, and re-establish the continuity of

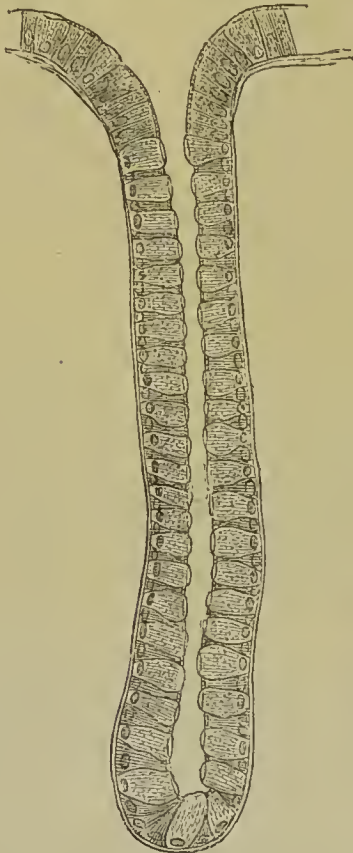


Fig. 239.

Lieberkühn's gland from the large intestine (dog).

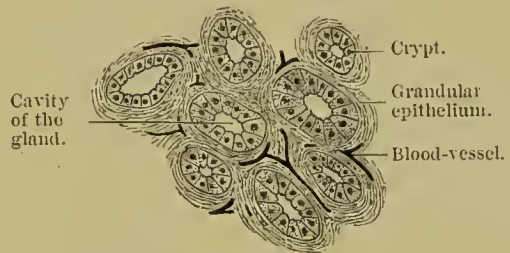


Fig. 240.

Transverse section of Lieberkühn's follicles.

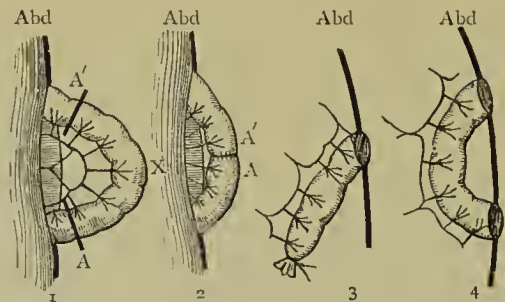


Fig. 241.

Scheme of Thiry's fistula. 1, 2, 3, 4, Vella's fistula. AA' are stitched together; Abd., Abdominal wall (*Stirling*).

the rest of the intestine. Stitch *both* ends of the loop of intestine into the wound in the linea alba (fig. 241, 4), so that there is a loop of intestine supplied by its blood-vessels and nerves, isolated, and with an upper and lower aperture.]

The intestinal juice of such fistulæ flows spontaneously in very small amount, and is increased during digestion; it is increased—especially its mucus—by mechanical, chemical, and electrical stimuli; at the same time, the mucous membrane becomes red, so that 100 centimetres yield 13 to 18 grams of this juice in a hour (*Thiry*). The juice is light yellow, opalescent, thin, strongly alkaline; specific gravity 1011; evolves CO_2 when an acid is added; it contains albumin, ferments, and mucus—especially the juice of the large intestine. Its composition is—water, 97.59; proteids, 0.80; other organic substances = 0.73; salts, 0.88 per cent.; amongst these—sodium carbonate, 0.32 to 0.34 per cent.

[The intestinal juice obtained by Meade Smith's method contained only 0.39 per cent. of organic matter, and in this respect agreed closely with the juice which A. Moreau procured by dividing the mesenteric nerves of a ligatured loop of intestine. The secretion of the large intestine is much more viscid than that of the small intestine.]

[Very discordant results as to the quantity and actions of the intestinal juice have been obtained by different observers. Rohmann, however, working with a Vella's fistula finds that the quantity of secretion obtained depends on the position of the loop of intestine isolated, more fluid being obtained from the lower than from the upper portion of the gut. The fluid of the upper portions yields much diastatic ferment, that of the lower only traees. Invertin is found in the upper but not in the lower portions. Demant collected some human intestinal juice, but he found that it had no action on fibrin, and only a slight action on boiled starch.]

Actions of Succus Entericus.—It is most active in the dog, and in other animals it is more or less inactive.

(1) It is less diastatic than the saliva and the pancreatic juice, but it does not form maltose; while the juice of the large intestine does not possess this property (*Eichhorst*).

(2) It converts maltose into grape-sugar. It seems, therefore, to continue the diastatic action of saliva (§ 148) and pancreatic juice (§ 170), which usually form only maltose.

According to Bourquelot this action is due to the intestinal schizomycetes and not to the intestinal juice as such, the saliva, gastric juice, or invertin. The greater part of the maltose appears, however, to be absorbed unchanged.

(3) Fibrin is slowly (by the trypsin and pepsin—*Kühne*) peptonised (*Thiry, Leube*); less easily albumin (*Masloff*), fresh casein, flesh raw or cooked, vegetable albumin; probably gelatin also is changed by a special ferment into a solution which does not gelatinise (*Eichhorst*).

(4) Fats are only partly emulsified (*Schiff*), and afterwards decomposed (*Vella*).

(5) According to Cl. Bernard **invertin** occurs in intestinal juice (this ferment can also be extracted from yeast). It causes cane-sugar ($C_{12}H_{22}O_{11}$) to take up water (+ H_2O), and converts it into invert-sugar, which is a mixture of left rotating sugar (lævulose, $C_6H_{12}O_6$) and of grape-sugar (dextrose, $C_6H_{12}O_6$) (p. 342). Heat seems to be absorbed during the process.

[Hoppe-Seyler has suggested that this ferment is not a natural product of the body, but is introduced from without with the food. Matthew Hay, however, finds it to be invariably present in the small intestine of the fetus.]

[Bunge suggests that as it is doubtful if it has any digestive action on food, that its chief importance lies in the sodic carbonate which it contains. This substance neutralises the acids of the intestinal contents, and helps to emulsify the fats.]

[Effect of Drugs on the Succus Entericus.]—The subcutaneous injection of pilocarpin causes the mucous membrane of a Vella's fistula to be congested, when a strongly alkaline, opalescent, watery, and slightly albuminous secretion is obtained. This secretion produces a reducing sugar, converts cane-sugar into invert-sugar, emulsifies neutral fats, ultimately splitting them up, peptonises proteids, and coagulates milk, even although the milk be alkaline. The juice attacks the sarcous substance of muscle before the connective-tissues—the reverse of the gastric juice. The mucous membrane in a Vella's fistula does not atrophy. K. B. Lehmann finds that the succus entericus obtained from the intestine of a goat by a Vella fistula has no digestive action.]

The Action of Nerves on the secretion of the intestinal juice is not well determined. Section or stimulation of the vagi has no apparent effect; while extirpation of the large sympathetic abdominal ganglia causes the intestinal canal to be filled with a watery fluid, and gives rise to diarrhoea. This may be explained by the paralysis of the vaso-motor nerves, and also by the section of large lymphatic vessels during the operation, whereby absorption is interfered with and transudation is favoured. **Moreau's Experiment**—Moreau placed four ligatures on a loop of intestine at equal distances from each other (fig. 242). The ligatures were tied so that three loops of intestine were shut off. The nerves (N) to the middle loop were divided, and the intestine was replaced in the abdominal cavity. After a time, a very small amount of secretion, or none at all, was found in two of the ligatured compartments of the gut, i.e., in those with the nerves and blood-vessels intact (1, 3), but the compartment (2) whose nerves had been divided contained a watery secretion. Perhaps the secretion which occurs

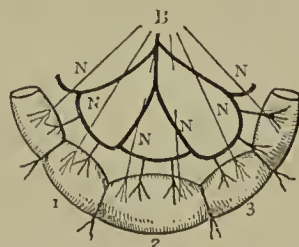


Fig. 242.

Scheme of Moreau's experiment (*Stirling*).

after section of the mesenteric nerves is a paralytic secretion. The secretion of the intestinal and gastric juices is **diminished** in man in certain nervous affections (hysteria, hypochondriasis, and various cerebral diseases); while in other conditions these secretions are increased.

Excretion of Drugs.—If an isolated intestinal fistula be made, and various drugs administered, the mucous membrane excretes iodine, bromine, lithium, sulphocyanides, but *not* potassium ferrocyanide, arsenious or boracic acid, or iron salts.

In **sucklings**, not unfrequently a large amount of acid is formed, when the fungi in the intestine split up milk-sugar or grape-sugar into lactic acid (*Leube*). Starch changed into grape-sugar may undergo the same abnormal process; hence, infants ought not to be fed with starchy food.

Fate of the digestive Ferments.—Langley is of opinion that the digestive ferments are destroyed in the intestinal canal; the diastatic ferment of saliva is destroyed by the free HCl of the gastric juice; pepsin and rennet are acted upon by the alkaline salts of the pancreatic and intestinal juices, and by trypsin; while the diastatic and peptic ferments of the pancreas disappear under the influence of the acid fermentation in the large intestine. (See Urine, § 262.)

184. FERMENTATION IN THE INTESTINE.—Those processes, which are to be regarded as fermentations or putrefactive processes, are quite different from those caused by the digestive enzymes or ferments just considered. [Lea proposes the term **zymolysis** for the changes brought about by unorganised ferments, in contradistinction to the results produced by organised ferments, such as yeast, or various bacteria.] The **putrefactive changes** are connected with the presence of lower organisms, so-called fermentation- or putrefaction-producers: and they may develop in suitable media outside the body. The lowly organisms which cause the intestinal fermentation are swallowed with the food and drink, and also with the saliva. When they are introduced, fermentation and putrefaction begin, and *gases are evolved*.

Intestinal Gases.—During the whole of the foetal period, until birth, fermentation cannot occur; hence gases are never present in the intestine of the newly-born. The first air-bubbles pass into the intestine with the saliva which is swallowed, even before food has been taken. The germs of organisms are thus introduced into the intestine, and give rise to the formation of gases. The evolution of intestinal gases goes hand in hand with the fermentations. Air is also swallowed, and an exchange of gases takes place in the intestine, so that the composition of the intestinal gases depends upon various conditions. Kolbe and Ruge collected the gases from the anus of a man, and found in 100 vols. :—

Food.	CO ₂ .	H.	CH ₄ .	N.	H ₂ S.
Milk, . . .	16·8	43·3	0·9	38·3	Quantity not estimated.
Flesh, . . .	12·4	2·1	27·5	57·8	
Peas, . . .	21·0	4·0	55·9	18·9	

1. Air-bubbles are swallowed with the food. The O is rapidly absorbed in the intestinal tract, so that in the lower part of the large intestine, even traces of O are absent. In exchange, the blood-vessels in the intestinal wall give off CO₂ into the intestine, so that part of the CO₂ in the intestine is derived by diffusion from the blood.

2. H, CO₂, NH₃, and CH₄ are also formed from the intestinal contents by fermentation, which takes place even in the small intestine.

Fungi.—The chief agents in the production of fermentations, putrefaction, and other similar decompositions are undoubtedly the group of fungi called **fission fungi** or **schizomycetes**. They are small unicellular organisms of various forms—globular, *micrococcus*; short rods, *bacterium*; long rods, *bacillus*; or spiral threads, *vibrio*, *spirillum*, *spirochaeta* (fig. 32). The mode of reproduction is by division, and they may either remain single or unite to form colonies. Each organism is usually capable of some degree of motion. They produce profound chemical changes in the fluids or media in which they grow and multiply, and these changes depend upon the vital activity of their protoplasm. These minute microscopic organisms take

certain constituents from the "nutrient fluids" in which they live, and use them partly for building up their own tissues and partly for their own metabolism. In these processes, some of the substances so absorbed and assimilated undergo chemical changes, some *ferments* seem thereby to be produced, which in their turn may act upon material present in the nutritive fluid.

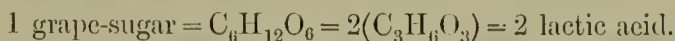
These fungi consist of a **capsule** enclosing **protoplasmic contents**. Many of them are provided with excessively delicate cilia, by means of which they move about. The new organisms, produced by the division of pre-existing ones, sometimes form large colonies visible to the naked eye, the individual fungi being united by a jelly-like mass, the whole constituting **zoogloea**. In some fungi, reproduction takes place by **spores**; more especially when the nutrient fluids are poor in nutritive materials. The bacteria form longer rods or threads, which are jointed, and in each joint or segment small ($1-2\ \mu$) highly refractive globules or *spores* are developed (fig. 243, 7). In some cases, as in the butyric acid fermentation, the rods become fusiform before spores are formed. When

the envelope of the mother-cell is ruptured or destroyed, the spores are liberated, and if they fall upon or into a suitable medium, they germinate and reproduce organisms similar to those from which they sprang. The process of **spore-production** is illustrated in fig. 243 B, 7, 8, 9, and in 1, 2, 3, 4 is shown the process of **germination** in the butyric acid fungus. The spores are very tenacious of life; they may be dried, when they resist death for a very long time; some of them are killed by being boiled. Some fungi exhibit their vital activities only in the presence of O (*aerobes*), while others require the exclusion of O (*anærobes*, *Pasteur*). According to the products of their action, they are classified as follows:—

Those that produce **fermentations** (*zymogenic schizomycetes*); those that produce **pigments** (*chromogenic*); those that produce disagreeable odours, as during putrefaction (*bromogenic*); and those that, when introduced into the living tissues of other organisms, produce **pathological conditions**, and even death (*pathogenic*). All these different kinds occur in the human body.

When we consider that numerous fungi are introduced into the intestinal canal with the food and drink—that the temperature and other conditions within this tube are specially favourable for their development; that there also they meet with sufficient pabulum for their development and reproduction—we cannot wonder that a rich crop of these organisms is met with in the intestine, and that they produce there numerous fermentations.

I. Fermentation of Carbohydrates.—(1) *Bacillus acidi lactici* consists of biscuit-shaped cells, $1.5-3\ \mu$ in length, arranged in groups or isolated. They split up grape-sugar into lactic acid:—



Milk-sugar ($\text{C}_{12}\text{H}_{22}\text{O}_{11}$) can be split up by the same ferment, causing it to take up H_2O , and forming 2 molecules of grape-sugar, $2(\text{C}_6\text{H}_{12}\text{O}_6)$, which are again split into 4 molecules of lactic acid $4(\text{C}_3\text{H}_6\text{O}_3)$.

This fungus and its spores occur everywhere in the atmosphere, and are the cause of the spontaneous acidification and subsequent coagulation of milk (§ 230). There are other lactic acid-forming fungi.

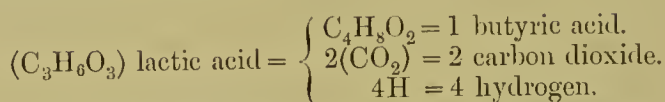
(2) *Bacillus butyricus*, which in the presence of starch is often coloured blue



Fig. 243.

A, *Bacterium aceti* in the form of—cocci (1); diplococci (2); short rods (3); and jointed threads (4, 5). B, *Bacillus butyricus*—(1) isolated spore; (2, 3, 4) germinating condition of the spores; (5, 6) short and long rods; (7, 8, 9) formation of spores within a cellular fungus.

by iodine, changes lactic acid into butyric acid, together with CO_2 and H (*Prazmowski*).



This fungus (fig. 243, B) is a true anaerobe, and grows only in the absence of O . The lactic acid fungus uses O very largely, and is, therefore, its natural precursor. The butyric acid fermentation is the last change undergone by many carbohydrates, especially by starch and inulin. It takes place constantly in the feces. Some other fungi have a similar action.

(3) Certain **micrococci** cause *alcohol* to be formed from carbohydrates. The presence of **yeast** may cause the formation of alcohol in the intestine, and in both cases also from milk-sugar, which first becomes changed into dextrose.

(4) **Bacterium aceti** (fig. 243, A) converts alcohol into acetic acid outside the body. Alcohol ($\text{C}_2\text{H}_6\text{O}$) + O = $\text{C}_2\text{H}_4\text{O}$ (Aldehyd) + H_2O . Acetic acid ($\text{C}_2\text{H}_4\text{O}_2$) is formed from aldehyd by oxidation. According to Nägeli, the same fungus causes the formation of a small amount of CO_2 and H_2O . As the acetic fermentation is arrested at 35°C ., this fermentation cannot occur in the intestine, and the acetic acid, which is constantly found in the feces, must be derived from another source. During putrefaction of the proteids, with exclusion of air, acetic acid is produced (*Nencki*).

(5) **Starch** and **cellulose** are partly *dissolved* by the schizomycetes (*Bac. butyricus* and *Vibrio rugula*) of the intestine. If cellulose be mixed with cloacal-mucus, or with the contents of the intestine, it passes into a saccharine carbohydrate which decomposes into equal volumes of CO_2 and CH_4 (*Hoppe-Seyler*).

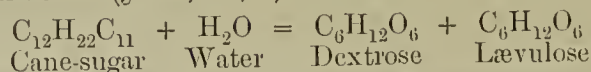
When the cellulose envelopes are softened and dissolved the digestive juices can act upon the enclosed digestible parts of the grains (*Tappeiner*).

[**Digestion of Cellulose.**—In **herbivora** 40–60 per cent. of the cellulose taken in the food disappears in the intestine. None of the digestive juices can digest cellulose so long as putrefaction does not take place in the digestive mixture. The maceration of the cellulose with saliva begins in the paunch, but the chief change takes place in the cæcum. It seems that first a sugar-like body is formed, and afterwards this may be split up into CO_2 and CH_4 . The putrefaction of cellulose yields large quantities of CO_2 and CH_4 .]

[Weiske found that he could digest a considerable quantity of the wood-fibres or cellulose of carrots, cabbage, and celery, but it can scarcely be regarded as a food for man. It however acts as a mechanical stimulus to promote peristalsis of the intestine. Hence it is absolutely essential for animals with a long intestine, *e.g.*, rabbits. A rabbit fed on food free from cellulose rapidly dies, because the onward movement of the intestinal contents ceases. If horn-parings be added to the food—which are quite indigestible—nutrition is normal in rabbits; they act in a purely mechanical manner in place of the cellulose (*Knieriem*).]

(6) Fungi, whose nature is unknown, can partly transform *starch* (?) and cellulose) into sugar.

(7) Others produce the ferment **invertin**. Invertin can change cane-sugar, milk-sugar, and maltose into glucoses (dextrose, lævulose, galactose) (§ 183, II., 5). Yeast has a similar action (§ 183, II., 5).



II. Fermentation of Fats (§ 251).—During putrefaction, organisms of an unknown nature cause neutral fats to take up water and split into glycerin and their corresponding fatty acid (§ 170). **Glycerin** is capable of undergoing several fermentations, according to the fungus which acts upon it (§ 251). With a neutral reaction, in addition to succinic acid, a number of fatty acids, H and CO_2 are formed.

Fitz found that the *hay-bacillus* (*Bacillus subtilis*, fig. 244) formed alcohol, and caproic, butyric, and acetic acids; in other cases, especially butyric alcohol, van de Velde found butyric, lactic, and traces of succinic acid with CO_2 , H_2O , N .

The **fatty acids**, especially as chalk soaps, form an excellent material for fermen-

tation. Calcium formiate mixed with cloacal-mucus ferments and yields calcium carbonate, CO_2 and H ; calcium acetate, under the same conditions, produces calcium carbonate, CO_2 and CH_4 . Amongst the *oxy-acids*, we are acquainted with the fermentations of lactic, glycerinic, malic, tartaric, and citric acids.

According to Fitz, *lactic acid* (in combination with chalk) produces propionic and acetic acids, CO_2 , H_2O . Other ferments cause the formation of valerianic acid. *Glycerinic acid*, in addition to alcohol and succinic acid, yields chiefly acetic acid; *malic acid* forms succinic and acetic acid. The other acids above enumerated yield somewhat similar products.

III. Fermentation of Proteids (§ 249).—The undigested proteids and their derivatives appear to be acted upon by fungi. Many fission fungi (*Bac. subtilis* and the spirillum

of cheese), however, can produce a *peptonising ferment*, so that a small amount of the peptonising done in the intestine may be due to microbes. This however has not been proved, although it has been rendered probable by the experiments of Vignal.

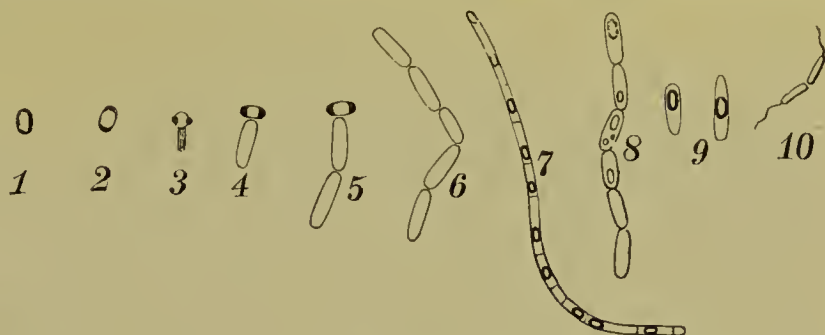


Fig. 244.

Bacillus subtilis. 1, spore; 2, 3, 4, its germination; 5, 6, short rods; 7, jointed thread, with the formation of spores in each segment; 8, short rods, some of them containing spores; 9, spores in single short rods; 10, fungus with a cilium.

We have already seen that pancreatic digestion acts upon the proteids, forming, among other products, amido-acids, leucin, tyrosin, and other bodies (§ 170, II.). Under normal conditions, this is the greatest decomposition produced by the pancreatic juice. The putrefactive fermentation of the large intestine causes further and more profound decompositions. **Leucin** ($\text{C}_6\text{H}_{13}\text{NO}_2$) takes up two molecules of water and yields valerianic acid ($\text{C}_5\text{H}_{10}\text{O}_2$), ammonia, CO_2 and H_4 ; **glycin** behaves in a similar manner. **Tyrosin** ($\text{C}_9\text{H}_{11}\text{NO}_3$) is decomposed into **indol** ($\text{C}_8\text{H}_7\text{N}$), which is constantly present in the intestine along with carbon dioxide, water, and H . If O be present, other decompositions take place. These putrefactive products are absent from the intestinal canal of the foetus and the newly-born. During the putrefactive decomposition of proteids, CO_2 , H_2S , H , and CH_4 , are formed; the same result is obtained by boiling them with alkalis. **Gelatin**, under the same conditions, yields much leucin and ammonia, CO_2 , acetic, butyric, and valerianic acids, and glycin. Mucin and nuclein undergo no change. Artificial pancreatic digestion-mixtures rapidly tend to undergo putrefaction.

The substance which causes the peculiar *fæcal odour* is produced by putrefaction, but its nature is not known. It clings so firmly to indol and skatol that these substances were formerly regarded as the odorous bodies, but when they are prepared pure they are odourless (*Bayer*).

Amongst the solid substances in the large intestine formed *only by putrefaction* is **indol** ($\text{C}_8\text{H}_7\text{N}$), a substance which is also formed when proteids are heated with alkalis, or by superheating them with water to 200°C . It is the stage preceding the indican in the urine. If the products of the digestion of the proteids—the peptones—are rapidly absorbed, there is only a slight formation of indol; but when absorption is slight, and putrefaction of the products of pancreatic digestion occurs, much indol is formed, and indican appears in the urine.

Jaffé found much indican in the urine in strangulated hernia, and when the small intestine was obstructed (§ 262, 1).

Reactions for Indol.—Acidulate strongly with HCl, and shake vigorously after adding a few drops of turpentine. If there be an intense red colour, the pigment is removed by ether. The substance—**protein-chromogen**—which is formed after the digestion of fibrin by trypsin, and which gives a violet colour with bromine water (§ 170, II.), can be removed by chloroform. In addition to the last pigment, there is a second one, which passes over during distillation, and which can be extracted from the distillate by ether. Both substances seem to belong to the indigo group (*Krukenberg*).

A. Bayer prepared indigo-blue artificially from ortho-phenyl-propionic acid, by boiling with dilute caustic soda, after the addition of a little grape-sugar. He obtained indol and skatol from indigo-blue. Hoppe-Seyler found that on feeding rabbits with ortho-nitrophenyl-propionic acid, much indican was present in the urine.

Phenol (C_6H_6O) is formed during putrefaction in the intestine, and it is also formed when fibrin and pancreatic juice putrefy outside the body, while Brieger found it constantly in the fæces. It seems to be increased by the same circumstances that increase indol, as an excess of indican in the urine is accompanied by an increase of phenylsulphuric acid in that fluid (§ 262).

From putrefying flesh and fibrin, amido-phenylpropionic acid is obtained, as a decomposition-product of tyrosin. A part of this is transformed by putrefactive ferments into hydrocinnamic acid (phenylpropionic acid). The latter is completely oxidised in the body into benzoic acid, and appears as hippuric acid in the urine. Thus is explained the formation of hippuric acid from a purely albuminous diet.

Skatol (C_9H_9N = methylindol) is a constant human fæcal substance, and has been prepared artificially by Nencki and Secretan from egg-albumin, by allowing it to putrefy for a long time under water. It also appears in the urine as a sulphur compound. The **excretin** of human fæces, described by Marcet, is related to cholesterin, but its history and constitution are unknown.

According to Salkowski, skatol and indol are both formed from a common substance which exists preformed in albumin, and which, when it is decomposed, at one time yields more indol, at another skatol, according as the hypothetical "*indol fungus*," or "*skatol fungus*," is the more abundant.

It is of the utmost importance, in connection with the processes of putrefaction, to determine whether they take place when oxygen is excluded, or not. When O is absent, **reductions** take place; oxy-acids are reduced to fatty acids, and hydrogen, marsh gas, and H_2S are formed; while the H may produce further reductions. If O be present, the nascent H separates the molecule of free ordinary oxygen ($= O_2$) into two atoms of active oxygen ($= O$). Water is formed on the one hand, while the second atom of O is a powerful oxidising agent (*Hoppe-Seyler*).

It is remarkable that the putrefactive processes, after the development of phenol, indol, skatol, cresol, phenylpropionic and phenylacetic acids are subsequently limited, and after a certain concentration of the fluid with these bodies is reached, the putrefactive processes cease altogether. The putrefactive process produces antiseptic substances which kill the micro-organisms, so we may assume that these substances limit to a certain extent the putrefactive processes in the intestine.

The **reaction** of the **small intestine** immediately below the stomach is acid, but the pancreatic and intestinal juices cause a neutral and afterwards an alkaline reaction, which obtains along the whole small intestine. In the **large intestine**, the reaction of its wall is alkaline, but the contents are generally acid, on account of the acid fermentation and the decomposition of the ingesta and the fæces.

[Rôle of micro-organisms in the intestine.]—It is to be remembered that micro-organisms exist throughout the entire intestinal tract. Numerous microbes have been found in the saliva (p. 253), stomach (p. 349), and small intestine (p. 340). From the normal intestinal mucus Babes has isolated five species of bacteria, while an enormous number of micro-organisms exist in the large intestine and fæces (p. 347). Vignal calculates their number at 20 millions per decigram of fæces. All these organisms resist the action of the digestive juices, save a few which are dissolved by the gastric juice.

The researches of Duclaux, Vignal, and others have shown that certain of these

micro-organisms secrete soluble ferments identical in their action with the ferments of the digestive juices. Vignal states that certain of these organisms contribute to the dissolution of food in the intestine. It is certain that they contribute to many processes of fermentation and decomposition which go on in the intestine. During foetal life these organisms are wanting, but they are numerous a few days after birth (*Beaunis*). In this connection one cannot fail to remember that bacteria by their action can produce in albuminous fluids albumoses and peptones, and that the former bodies are now regarded by bacteriologists as substances which play an important rôle in many pathological processes.]

185. PROCESSES IN THE LARGE INTESTINE.—Within the large intestine, the fermentative and putrefactive processes are certainly more prominent than the digestive processes proper, as only a very small amount of the intestinal juice is found in it. The **absorptive function** of the large intestine is greater than its secretory function, for at the beginning of the colon its contents are thin and watery, but in the further course of the intestine they become more solid. Water and the products of digestion in solution are not the only substances absorbed, but under certain circumstances, unchanged fluid egg-albumin, milk and its proteids, flesh juice, solution of gelatin, myosin with common salt, may also be absorbed. Experiments with acid-albumin, syntonin, or blood-serum gave no result. Toxic substances are certainly absorbed more rapidly than from the stomach. [In the dog the secretion of the large intestine has no digestive properties, but fats are absorbed in it. Klug and Koreek regard its Lieberkühnian glands not as secreting- but as absorbing-structures.] The faecal matters are *formed* or rather *shaped* in the lower part of the gut. The caecum of many animals, *e.g.*, rabbit, is of considerable size, and in it fermentation seems to occur with considerable energy, giving rise to an acid-reaction. In man, the chief function of the caecum is absorption, as is shown by the great number of lymphatics in its walls. From the lower part of the small intestine and the caecum onwards, the ingesta assume the faecal odour.

[Heidenhain found that in an excised loop of intestine, as in a Vella's fistula, but where the two ends of the loop were stitched together and returned to the abdomen, after several weeks the closed loop of gut was found to contain a fecal-like mass. It is evident, therefore, that the secretion of the large intestine must contribute matters to the faeces.]

The **amount of faeces** is about [5 oz. or] 170 grms. (60 to 250 grms.) in twenty-four hours; but if much indigestible food be taken, it may be as much as 500 grms. The amount is less, and the absolute amount of solids is less, after a diet of flesh and albumin, than after a vegetable diet. The faeces are rendered lighter by the evolution of gases, and hence they float in water.

The **consistence** depends on the amount of water present—usually about 75 per cent. The amount of water depends partly on the food—pure flesh diet causes relatively dry faeces, while substances rich in sugar yield faeces with a relatively large amount of water. The quantity of water taken has no effect upon the amount of water in the faeces. But the energy of the peristalsis has. The more energetic the peristalsis is, the more watery the faeces are, because sufficient time is not allowed for absorption of the fluid from the ingesta. Paralysis of the blood- and lymph-vessels, or section of the nerves, leads to a watery condition of the faeces (§ 183).

The **reaction** is often acid, in consequence of lactic acid being developed from the carbohydrates of the food. Numerous other acids produced by putrefaction are also present (§ 184). If much ammonia be formed in the lower part of the intestine, a neutral or even alkaline reaction may obtain. A copious secretion of mucus favours the occurrence of a neutral reaction.

The **odour**, which is stronger after a flesh diet than after a vegetable diet, is

caused by some faecal products of putrefaction, which have not yet been isolated ; also by volatile fatty acids and by sulphuretted hydrogen, when they are present.

The **colour** of the fæces depends upon the amount of altered bile-pigments mixed with them, whereby a bright yellow to a dark brown colour is obtained.

The colour of the food is also of importance. If much blood be present in the food, the fæces are almost brownish-black from hæmatin ; green vegetables = brownish-green from chlorophyll ; bones (*dog*) = white from the amount of lime ; preparations of iron = black from the formation of sulphide of iron.

The fæces contain—

(1) The **unchanged residues** of animal or vegetable tissues used as food ; hairs, horny and elastic tissues ; most of the cellulose, woody fibres, spiral vessels of vegetable cells, gums.

(2) **Portions of digestible substances**, especially when these have been taken in too large amount, or when they have not been sufficiently broken up by chewing. Portions of muscular fibres, ham, tendon, cartilage, particles of fat, coagulated albumin—vegetable cells from potatoes and other vegetables, raw starch, &c. (fig. 245).

All food yields a certain amount of residue—white bread, 3·7 per cent. ; rice, 4·1 per cent. ; flesh, 4·7 per cent. ; potatoes, 9·4 per cent. ; cabbage, 14·9 per cent. ; black bread, 15 per cent. ; yellow turnip, 20·7 per cent. (*Rubner*).

(3) The **decomposition-products** of the bile-pigments, which do not now give

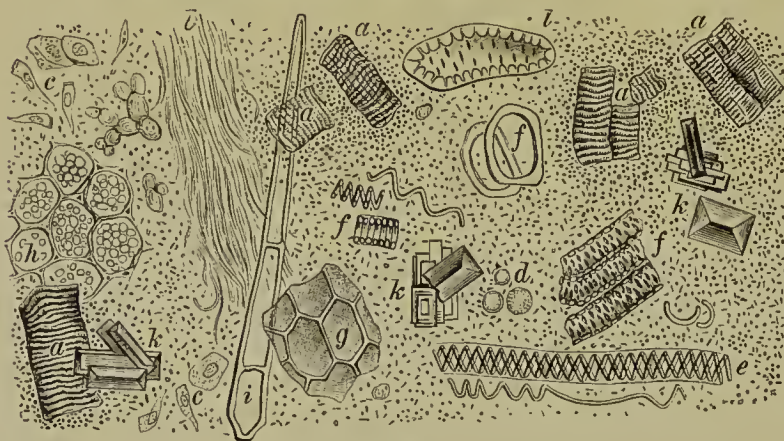


Fig. 245.

Fæces. *a*, muscular fibres ; *b*, tendon ; *c*, epithelium ; *d*, leucocytes ; *e-i*, different forms of vegetable cells and between the whole numerous bacteria, *l*. Between *h* and *b*, yeast ; *k*, triple phosphate.

Gmelin's reaction ; as well as the altered bile-acids (§ 177, 2). This reaction, however, may be obtained in pathological stools, especially in those of a green colour ; unaltered bilirubin, biliverdin, glycocholic and taurocholic acids occur in meconium (§ 182).

no unchanged bile-pigments in the fæces. A substance called **stercobilin** is obtained from the fæces, and it closely resembles what has been called "febrile" urobilin, but it is certainly different from normal urobilin.]

(4) **Unchanged mucin and nuclein**—the latter occasionally after a diet of bread, together with partially disintegrated cylindrical epithelium from the intestinal canal, and occasionally drops of oil. Cholesterin is very rare. [Ten grains of a substance, **stercorin**, said to be a modification of cholesterin, occur in the fæces (*Flint*).] The less the mucus is mixed with the fæces, the lower the part of the intestine from which it is derived (*Nothnagel*).

(5) After a milk diet, and also after a fatty diet, crystalline needles of lime combined with fatty acids and chalk soaps constantly occur, even in sucklings (*Wegscheider*). Even unchanged masses of casein and fat occur during the milk cure. Compounds of ammonia, with the acids mentioned as the result of putrefaction (§ 184, III.), belong to the faecal matters (*Brieger*).

(6) Amongst **inorganic residues**, soluble salts rarely occur in the fæces because they diffuse readily, *e.g.*, common salt, and the other alkaline chlorides, the compounds of phosphoric acid, and some of those of sulphuric acid. The **insoluble compounds**—of which ammoniaco-magnesian or triple phosphate (fig. 245, *k*), neutral calcic phosphate, yellow-coloured lime salts, calcium carbonate, and magnesium phosphate are the chief—form 70 per cent. of the ash. Some of these insoluble substances are derived from the food, as lime from bones, and in part they are excreted after the food has been digested, as ashes are eliminated from food which has been burned.

Concretions.—The excretion of inorganic substances is sometimes so great that they form incrustations around other faecal matters. Usually ammoniaco-magnesian phosphate occurs in large crystals by itself, or it may be mixed with magnesium phosphate.

(7) **Micro-organisms.**—A considerable portion of normal faecal matter consists of micrococci and microbacteria; yeast is seldom absent (*Frerichs, Nothnagel*).

To isolate the individual fungi, Escherich has made **pure cultivations** from the intestinal contents of sucklings, and Bienstock from adults. In the intestine of **sucklings** which have

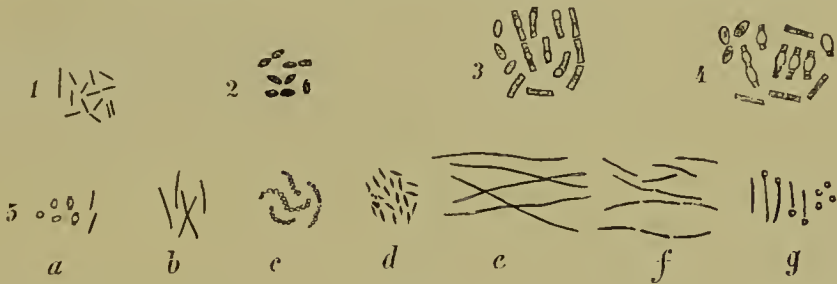


Fig. 246.

1, *Bacterium coli commune*; 2, *Bacterium lactis aërogenes*; 3 and 4, the large bacilli of Bienstock, with partial endogenous spore-formation; 5, the various stages in the development of the bacillus which causes the fermentation of albumin.

been nourished entirely on their mother's milk, the *Bacterium lactis aërogenes* (fig. 246, 2) causes the lactic acid fermentation and the evolution of CO_2 and H_2 in the upper part of the canal where some milk-sugar is still unabsorbed. In the **evacuations** is the characteristic slender *Bacterium coli commune* (fig. 246, 1). In addition, occasionally there are other bacilli, cocci, spores of yeast, and a mould.

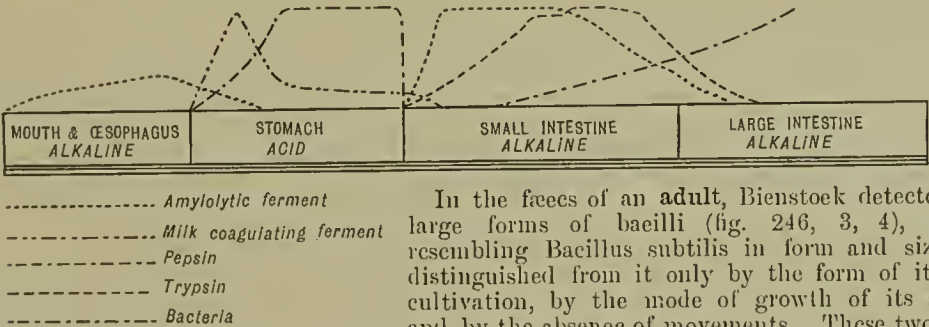


Fig. 247.

Reaction of the contents of the intestinal tract.

small, very slowly-developing bacillus occurs in three-fourths of all stools. A fourth kind (absent in sucklings) is the specific bacillus (§ 184, III.), causing the decomposition of albumin, resulting in the products of putrefaction and a faecal odour. This is the only bacillus that excites these processes in the intestine; but it does not decompose casein and alkali-albumin. In fig. 246, 5, *a-g*, the stages in the development of this bacillus are represented, but the stages from *c* to *g* are absent in the fæces, and are found only in artificial cultivations.

In the fæces of an **adult**, Bienstock detected two large forms of bacilli (fig. 246, 3, 4), closely resembling *Bacillus subtilis* in form and size, but distinguished from it only by the form of its pure cultivation, by the mode of growth of its spores, and by the absence of movements. These two forms can be distinguished microscopically by the mode of their cultivation, which is either in the form of a grape or a flat membrane. These two do not excite a fermentative action. A third micrococcus-like,

If the feces are simply investigated microscopically and without special precautions, there are other fungi, some of which may be introduced through the anus. In stools that contain much starch, the *Bacillus butyricus*, which is tinged blue with iodine, occurs (§ 184), and other small globular or rod-like fungi, which give a similar reaction (*Nothnagel, Uffelmann*).

The changes of the intestinal contents have been studied on persons with an accidental intestinal fistula, or an artificial anus.

[The preceding scheme (fig. 247), from Krukenberg shows graphically the reaction of the contents of the various parts of the alimentary canal, and also the distribution of the ferments.]

186. PATHOLOGICAL VARIATIONS.—A. The taking of food may be interfered with by spasm of the muscles of mastication (usually accompanied by general spasms), stricture of the œsophagus, by cicatrices after swallowing caustic fluids (*e.g.*, caustic potash, mineral acids), or by the presence of a tumour, such as cancer. Inflammation of all kinds in the mouth or pharynx interferes with the taking of food. Inability to swallow occurs as part of the general phenomena in disease of the medulla oblongata, in consequence of paralysis of the motor centre (superior olives) for the facial, vagus, and hypoglossal nerves, and also for the afferent or sensory fibres of the glosso-pharyngeal, vagus, and trigeminals. Stimulation or abnormal excitation of these parts causes spasmodic swallowing, and the disagreeable feeling of a constriction in the gullet (*globus hystericus*).

B. The secretion of saliva is diminished during inflammation of the salivary glands; occlusion of their ducts by concretions (salivary calculi); also by the use of atropin, daturin, and during fever, whereby the secretory (not the vaso-motor) fibres of the chorda appear to be paralysed (§ 145). When the fever is very high, no saliva is secreted. The saliva secreted during moderate fever is turbid and thick and usually acid. As the fever increases, the diastatic action of the saliva diminishes. The secretion is increased by stimulation of the buccal nerves (inflammation, ulceration, trigeminal neuralgia), so that the saliva is secreted in great quantity. Mercury and jaborandi cause secretion of saliva, the former causing stomatitis, which excites the secretion of saliva reflexly. Even diseases of the stomach accompanied by vomiting cause secretion of saliva. A very thick tenacious sympathetic saliva occurs when there is violent stimulation of the vascular system during sexual excitement, and also during certain psychical conditions. The reaction of the saliva is acid in catarrh of the mouth; in fever, in consequence of decomposition of the buccal epithelium; and in diabetes mellitus, in consequence of acid fermentation of the saliva which contains sugar. Hence, diabetic persons often suffer from carious teeth. Unless the mouth of an infant be kept scrupulously clean, the saliva is apt to become acid.

C. Disturbances in the activity of the musculature of the stomach may be due to paralysis of the muscular layers, whereby the stomach becomes distended, and the ingesta remain a long time in it. A special form of paralysis of the stomach is due to non-closure of the pylorus (*Ebstein*). This may be due to disturbances of innervation of a central or peripheral nature, or there may be actual paralysis of the pyloric sphincter, or anæsthesia of the pyloric mucous membrane, which acts reflexly upon the sphincter muscle; and lastly, it may be due to the reflex impulse not being transferred to the efferent fibre within the nerve-centre. Abnormal activity of the gastric musculature hastens the passage of the ingesta into the intestine; vomiting often occurs.

D. Gastric digestion is delayed by violent bodily or mental exercise, and sometimes it is arrested altogether. Sudden mental excitement may have the same effect. These efforts are very probably caused through the vaso-motor nerves of the stomach. Feeble and imperfect digestion may be of a purely nervous nature (*Dyspepsia nervosa—Leube; Neurasthenia gastrica—Burkart*). An excessive formation of acid may be due to nervous disturbance, and is called "nervous gastroxynsis," by *Rosbach*.

[Action of Alcohol, Tea, &c., in Digestion.—According to J. W. Fraser, all infused beverages, tea, coffee, cocoa, retard the peptic digestion of proteids, with few exceptions. The retarding action is less with coffee than with tea. The tannic acid and volatile oil seem to be the retarding ingredients in teas. Distilled spirits—brandy, whisky, gin—have but a trifling retarding effect on the digestive processes; and when one considers their action on the secretory glands, it follows that in moderate dietetic doses they promote digestion. Wines are highly inimical to salivary digestion, but this is due to their acidity; and this effect can be removed by the addition of an alkali. Wines retard peptic digestion, the sparkling less than the still wines. Tea has an intensely inhibitory action on salivary digestion; in fact, a small quantity paralyses the action of saliva, while coffee has only a slight effect. This action of tea is due to the tannin. Tea, coffee, and cocoa all retard peptic digestion, when they form 20 per cent. of the digestive mixture (*W. Roberts*).]

[Action of bile on gastric digestion.—The passage of bile into the stomach in cases of gastric fistula in man, or the introduction of large quantities of bile into the stomach of dogs, contrary to what is usually stated, does not interfere with the gastric digestion of proteids (*Herzen, Dastre, Oddi*). Bile, however, added to artificial digests retards the process (p. 297).]

Inflammatory or catarrhal affections of the stomach, as well as ulceration and new forma-

tions, interfere with digestion, and the same result is caused by eating too much food which is difficult of digestion, or taking too much highly spiced sauce or alcohol. In the case of a dog suffering from chronic gastric catarrh, Grützner observed that the secretion took place continuously, and that the gastric-juice contained little pepsin, was turbid, sticky, feebly acid, and even alkaline. The introduction of food did not alter the secretion, so that in this condition the stomach really obtains no rest. The chief cells of the gastric-glands were turbid. Hence, in gastric catarrh, we ought to eat frequently, but take little at a time, while at the same time dilute hydrochloric acid ought to be administered (0·4 per cent.). Small doses of common salt seem to aid digestion.

[Absence of HCl.—HCl is almost always absent in carcinoma of the stomach (*van de Velde*), amyloid degeneration of the gastric mucous membrane (*Edinger*), and sometimes in fever. In all these cases the acid-reaction is due to lactic or butyric acid. The absence of HCl in cancer of the stomach is an important diagnostic and prognostic symptom. It is not absent in simple dilatation of the stomach. Test the contents of the stomach for free HCl with tropæolin (red colour), methyl-violet (blue), and with ferric chloride and carbolic acid (*Uffelmann*). $\frac{1}{10}$ per cent. of free HCl causes the amethyst-blue of the last to become steel-grey, while somewhat more discharges the colour altogether. [In testing for the presence of free lactic acid in the gastric contents use Uffelmann's reaction (§ 163). The lactic acid is easily extracted by ether from the gastric contents, and the reaction can then be performed with the residue obtained after evaporating the ether. A solution of 1 drop of the liquor perchloride in 50 c.c. of water is made yellow by lactic acid.]

Feeble digestion may be caused either by imperfect formation of acid or pepsin, so that both substances may be administered in such a condition. [It may also be due to deficient muscular power in the wall of the stomach.] In other cases, lactic, butyric, and acetic acids are formed, owing to the presence of lowly organisms. In such cases, small doses of salicylic acid, together with some hydrochloric acid, are useful. Pepsin need not be given often, as it is rarely absent, even from the diseased gastric mucous membrane. Albumin has been found in the gastric-juice in cases of gastric catarrh and cholera.

E. Digestion during Fever and Anæmia.—Beaumont found that in the case of Alexis St Martin, when fever occurred, a small amount of gastric-juice was secreted; the mucous membrane was dry, red, and irritable. Dogs suffering from septicæmic fever, or rendered anæmic by great loss of blood, secrete gastric-juice of feeble digestive power and containing little acid (*Manasséin*). [In acute diseases accompanied by fever, the inner cells of the fundus-glands of the human stomach may disappear (*C. Kupffer*).] Hoppe-Seyler investigated the gastric-juice of a typhus patient, in which van de Velde found no free acid. Usually no free hydrochloric acid is found in cancer of the stomach. The gastric-juice of the typhus patient did not digest artificially, even after the addition of hydrochloric acid. The diminution of acid, under these circumstances, favours the occurrence of a neutral reaction, so that, on the one hand, digestion cannot proceed, and on the other, fermentative processes (lactic and butyric acid fermentations with the evolution of gases) occur. These results are associated with the presence of micro-organisms and *Sarcina ventriculi* (*Goodsir*). Uffelmann found that the secretion of a peptone-forming gastric juice ceased in fever, when the fever is severe at the outset, when a feeble condition occurs, or when the temperature is very high. The amount of juice secreted is certainly diminished during fever. The excitability of the mucous membrane is increased so that vomiting readily occurs. The increased excitability of the vaso-motor nerves during fever is disadvantageous for the secretion of the digestive fluids (*Heidenhain*). Beaumont observed that fluids are rapidly absorbed from the stomach during fever, but the absorption of peptones is diminished on account of the accompanying catarrhal condition of the stomach, and the altered functional activity of the muscularis mucosæ (*Leube*).

Many salts, when given in large amount, disturb gastric digestion, e.g., the sulphates. While the alkaloids, morphia, strychnia, digitalin, narcotin, veratria have a similar action, quinine favours it (*Wolberg*). In some nervous individuals "peristaltic unrest of the stomach," conjoined with a dyspeptic condition, occurs (*Kussman*). [Prosser James directs attention to the value of peptic and pancreatic salts, which are preparations of common salt mixed with pepsin and the ferments of the pancreas respectively.]

[Artificial Digestion is affected by various salts, according to their nature and dilution. The digestion of fibrin by pepsin goes on best without the addition of salts, being diminished by magnesic sulphate, sodic carbonate, and sulphate. The digestion of fibrin by pancreatic extract is accelerated by sodic carbonate (*Heidenhain*), and retarded by MgSO_4 and Na_2SO_4 . The diastatic action of the saliva and pancreas on starch is greatly accelerated by NaCl (2 per cent.), while Na_2CO_3 , Na_2SO_4 , and MgSO_4 hinder it (*Pfeiffer*).] According to Schütz, artificial gastric digestion is retarded by a 2 per cent. solution of alcohol, and also by a solution of salicylic acid (·06 to ·1 per cent.). Buchner, however, finds that 10 per cent. of alcohol does not affect artificial gastric digestion, while above 20 per cent. arrests it. Beer hinders digestion.

F. In acute diseases, the secretion of bile is affected; it becomes less in amount and more watery, i.e., it contains fewer specific constituents. If the liver undergoes great structural change, the secretion may be arrested.

G. Gall-stones.—When decomposition of the bile occurs, gall-stones are formed in the *gall-bladder* or in the *bile-ducts*. Some are *white*, and consist almost entirely of stratified layers of crystals of *cholesterin*. The *brown* forms consist of bilirubin-lime, and calcium carbonate, often mixed with iron, copper, and manganese. The gall-stones in the gall-bladder become faceted by rubbing against each other. The nucleus of the white stones often consists of chalk and bile-colouring matters, together with nitrogenous residues, derived from shed epithelium, mucin, bile-salts, and fats. Gall-stones may occlude the bile-duct and cause cholera. When a small stone becomes impacted in a duct, it gives rise to excessive pain, constituting hepatic colic, and may even cause rupture of the bile-duct with its sharp edges.

H. Nothing certain has been determined regarding the **pancreatic secretion** in disease, but in fever it appears to be diminished in amount and digestive activity. The suppression of the pancreatic secretion, as by a cancerous tumour of the head of the pancreas, is often accompanied by the appearance of fat, in the form of globules or groups of crystals in the faeces.

I. Constipation is a most important derangement of the digestive tract. It may be caused by—(1) Conditions which *obstruct the normal channel*, *e.g.*, constriction of the gut from stricture—in the large gut after dysentery, tumours, rotation on its axis of a loop of intestine (volvulus), or invagination, occlusion of a coil of gut in a hernial sac, or by the pressure of tumours or exudations from without, or congenital absence of the anus. (2) Too great *dryness* of the contents, caused by too little water in the articles of diet, diminution of the amount of the digestive secretions, *e.g.*, of bile in icterus; or in consequence of much fluid being given off by other organs as after copious secretion of saliva, milk, or in fever. (3) Variations in the functional activity of the *muscles* and *motor-nervous apparatus* of the gut may cause constipation, owing to imperfect peristalsis. This condition occurs in inflammations, degenerations, chronic catarrh, and diaphragmatic inflammation. Affections of the spinal cord, and sometimes also of the brain, are usually accompanied by slow evacuation of the intestine. Whether diminished mental activity and hypochondriasis are the cause of, or are caused by, constipation is not proved. Spasmodic contraction of a part of the intestine may cause temporary retention of the intestinal contents, and, at the same time, give rise to great pain or colic; the same is true of spasm of the anal sphincter, which may be excited reflexly from the lower part of the gut. The faecal masses in constipation are usually hard and dry, owing to the water being absorbed; hence they form large masses or *scybalæ* within the large intestine, and these again give rise to new resistance. Amongst the reagents which prevent evacuation of the bowels, some paralyse the motor apparatus temporarily, *e.g.*, opium, morphia; some diminish the secretion of the intestinal mucous membrane, and cause constriction of the blood-vessels, as tannic acid, vegetables containing tannin, alum, chalk, lead acetate, silver nitrate, bismuth nitrate.

J. Increased *evacuation of the intestinal contents* is usually accompanied by a watery condition of the faeces, constituting **diarrhoea**. The causes are:—

1. A too rapid movement of the contents through the intestine, chiefly through the large intestine, so that there is not time for the normal amount of absorption to take place. The increased peristalsis depends upon stimulation of the motor-nervous apparatus of the intestine, usually of a reflex nature. Rapid transit of the contents through the intestine causes the evacuation of certain substances, which cannot be digested in so short a time.

2. The stools become thinner from the presence of much water, mucus, and the admixture with fat, and by eating fruit and vegetables. In rare cases, when the evacuations contain much mucin, Charcot's crystals occur (fig. 171, c). In ulceration of the intestine, leucocytes (pus) are present (*Nothnagel*).

3. Diarrhoea may occur as a consequence of disturbance of the diffusion-processes through the intestinal walls, as in affections of the epithelium, when it becomes swollen in inflammatory or catarrhal conditions of the intestinal mucous membrane. [Irritation over the abdomen, as from the subcutaneous injection of small quantities of saline solutions, causes diarrhoea.]

4. It may also be due to increased secretion into the intestine, as in capillary diffusion, when magnesium sulphate in the intestine attracts water from the blood.

The same occurs in cholera, when the stools are copious and of a rice-water character, and are loaded with epithelial cells from the villi. The transudation into the intestine is so great that the blood in the arteries becomes very thick, and may even on this account cease to circulate.

Transudation into the intestine also takes place as a consequence of paralysis of the vaso-motor nerves of the intestine. This is perhaps the case in diarrhoea following upon a cold. Certain substances seem directly to excite the secretory organs of the intestines or their nerves, such as the drastic purgatives (§ 180). Pilocarpin injected into the blood causes great secretion (*Masloff*).

During febrile conditions, the secretion of the intestinal glands seems to be altered quantitatively and qualitatively, with simultaneous alteration of the functional activity of the musculature and the organs of absorption, while the excitability of the mucous membrane is increased (*Uffelmann*). It is important to note that in many acute febrile diseases the amount of common salt in the urine diminishes, and increases again as the fever subsides.

187. COMPARATIVE.—**Salivary Glands.**—Amongst mammals, the herbivora have larger salivary glands than the carnivora; while midway between both are the omnivora. The whale

has no salivary glands. The pinnipedia have a small parotid, which is absent in echidna. The dog and many carnivora have a special gland lying in the orbit, the *orbital* or *zygomatic gland*. In birds the salivary glands open at the angle of the mouth, but the parotid is absent. Amongst reptiles the parotid of some species is so changed as to form poison-glands; the tortoise has sublingual glands; reptiles have labial glands. The amphibia and fishes have merely small glands scattered over the mouth. The salivary glands are large in insects; some of them secrete formic acid. The salivary glands are well developed in molluscs, and the saliva of *Dolium* galea contains more than 3 per cent. of free sulphuric acid (?). The cephalopods have a double set of glands.

A crop is not present in any mammal; the stomach is either *simple*, as in man, or, as in many rodents, it is divided into two halves, into a cardiac and a pyloric portion. The *intestine* is short in flesh-eating animals and long in herbivora. The stomach of ruminants is *compound*, and consists of four cavities. The first and largest is the *paunch* or *rumen*, then the *reticulum*. In these two cavities, especially the former, the ingesta are softened and undergo fermentation, they are then returned to the mouth by the action of the voluntary muscular fibres, which reach to the stomach. This is the process of *rumination*. The ingesta are chewed again in the mouth, and are again swallowed, but this time they enter the third cavity or *psalterium*—(which is absent in the camel)—and thence into the fourth stomach or *abomasum*, in which the fermentative digestion takes place. The cæcum is a very large and important digestive organ in herbivora and in most rodents; it is small in man, and absent in carnivora. The œsophagus in grain-eating birds not unfrequently has a blind diverticulum or *crop* for softening the food. In the crop of pigeons during the breeding season, there is formed a peculiar secretion—"pigeon's milk," which is used to feed the young (*J. Hunter*). The stomach consists of a glandular *proventriculus* and a strong *muscular stomach*, which is covered with horny epithelium and triturates the food. There are usually two fluid diverticula on the small intestine near where it joins the large gut. In fishes the intestinal canal is generally simple; the stomach is merely a dilatation of the tube; and at the pylorus there may be one, but usually many, blind glandular appendages (the appendices pyloricæ). They are generally longitudinal folds in the intestinal mucous membrane, but in some fishes, *e.g.*, the shark, there is a *spiral valve*. [The inversive cane-sugar ferment is wanting in the herbivora, as the cow, horse, and sheep, but is present in the dog and cat. It is also met with in birds and reptiles, and in many of the invertebrates, as the ordinary earth-worm (*M. Hay*).]

In *amphibia* and *reptiles* the stomach is a simple dilatation; the gut is larger in vegetable feeders than in flesh feeders. The *liver* is never absent in vertebrates, although the gall-bladder frequently is. [It is absent in the donkey, horse, elephant, and deer.] The *pancreas* is absent in some fishes.

Digestion in Plants.—The observations on the albumin-digesting power of some plants are extremely interesting (*Canby*, 1869; *Ch. Darwin*, 1875). The sundew or *drosera* has a series of tentacles on the surface of its leaves, and the tentacles are provided with glands. When an insect alights upon a leaf, it is suddenly seized by the tentacles; the glands pour out an acid juice over the prey, which is gradually digested, all except the chitinous structures. The secretion, as well as the subsequent absorption of the products of digestion, are accomplished by the activity of the protoplasm of the cells of the leaves. The digestive juice contains a pepsin-like ferment and formic acid. Similar phenomena are manifested by the Venus flytrap (*Dionæa*), by *pinguicula*, as well as by the cavity of the altered leaves of *Nepenthes*. About fifteen species of these "insectivorous" or carnivorous plants are known. Papain, and other ferments analogous in their action to trypsin, are referred to in § 170.

188. HISTORICAL.—**Digestion in the Mouth.**—The older observers regarded the *saliva* as a solvent, and in addition, many bad qualities, especially in starving animals, were ascribed to it. This arose from the knowledge of the saliva of mad animals, and the parotid saliva of poisonous snakes. The salivary glands have been known for a long time. Galen (131–203 A.D.) was acquainted with Wharton's duct and Aëtius (270 A.D.) with the sub-maxillary and sub-lingual glands. Hapel de la Chenaye (1780) obtained large quantities of saliva from a horse, in which he was the first to make a salivary fistula. Spallanzani (1786) asserted that food mixed with saliva was more easily digested than food moistened with water. Hamberger and Siebold investigated the reaction, consistence, and specific gravity of saliva, and found in it mucus, albumin, common salt, calcium and sodium phosphates. Berzelius gave the name *ptyalin* to the characteristic organic constituent of saliva, but Leuchs (1831) was the first to detect its diastatic action.

Gastric Digestion.—Digestion was formerly compared to "coction," whereby solution was effected. According to Galen, only substances that have been dissolved passed through the pylorus into the intestine. He described the movements of the stomach and the peristalsis of the intestines. Aclian gave names to the four stomachs of the ruminants. Vidius († 1567) noticed the numerous small apertures of the gastric glands. Van Helmont († 1644) expressly notices the *acidity* of the stomach. Reaumur (1752) knew that a juice was secreted by the stomach, which effected solution, and with which he and Spallanzani performed experiments on digestion

outside the body. Carminati (1785) found that the stomachs of carnivora during digestion secreted a very acid juice. Prout (1824) discovered the hydrochloric acid of the gastric-juice, Sprott and Boyd (1836) the glands of the gastric mucous membrane, while Wassmann and Bischoff noted the two kinds of gastric-glands. After Beaumont (1834) had made his observations upon Alexis St Martin, who had a gastric fistula caused by a gunshot wound, Bassow (1842) and Blondlot (1843) made the first artificial gastric-fistulae upon animals. Eberle (1830) prepared artificial gastric juice. Mialhe called albumin, when altered by gastric digestion albuminose; Lehmann, who investigated this substance more carefully, gave it the name *peptone*. Schwann isolated *pepsin* (1836), and established the fact of its activity in the presence of hydrochloric acid.

Pancreas, Bile, Intestinal Digestion.—The pancreas was known to the Hippocratic School; Maur. Hoffmann (1642) demonstrated its duct (fowl), and Wirsung described it in man. Regner de Graaf (1664) collected the pancreatic juice from a fistula, and Tiedemann and Gmelin found it to be alkaline, while Lauret and Lassaigne found that it resembled saliva. Valentin discovered its diastatic action, Eberle its emulsionising power, and Cl. Bernard (1846) its tryptic and fat-splitting properties. The last-mentioned function was referred to by Purkinje and Pappenheim (1836). Aristotle characterised the bile as a useless secretion; according to Erasistratus (304 B. C.), fine invisible channels conduct the bile from the liver into the gall-bladder. Arætaeus ascribed icterus to obstruction of the bile-duct. Benedetti (1493) described gall-stones. According to Jasolinus (1573), the gall-bladder is emptied by its own contractions. Sylvius noticed the lymphatics of the liver (1640); Walaeus, the connective tissue of the so-called capsule of Glisson (1641). Haller indicated the uses of bile in the digestion of fats. The liver-cells were described by Henle, Purkinje, and Dutrochet (1838). Heynsius discovered the urea and Cl. Bernard (1853) the sugar in the liver, and he and Hensen (1857) found glycogen in the liver. Kiernan gave a more exact description of the hepatic blood-vessels (1834). Beale injected the lymphatics, and Gerlach the finest bile-ducts. Schwann (1844) made the first biliary fistula; Demarcay particularly referred to the combination of the bile-acids with soda (1838); Strecker discovered the soda compounds of both acids, and isolated them. Celsus mentions nutrient enemata (3–5 A.D.). Fallopius (1561) described the *valvulae conniventes* and villi of the intestinal mucous membrane, and the nervous plexus of the mesentery. The agminated glands or patches of Peyer were known to Severinus (1645).

Physiology of Absorption.

189. THE ORGANS OF ABSORPTION.—[As most substances in the state in which they are used for food are either insoluble, or diffuse but imperfectly through membranes, the whole drift of the complicated digestive processes is to render these substances **soluble** and **diffusible**, and thus fit them for absorption; most of the neutral fats, however, are emulsified.]

The **mucous membrane** of the whole intestinal tract, as far as it is covered by a single layer of columnar epithelium, *i.e.*, from the cardiac orifice of the stomach to the anus—is adapted for absorption. The **mouth** and **œsophagus**, lined as they are by stratified squamous epithelium, are much less adapted for this purpose. Still, poisoning is caused by placing potassium cyanide in the mouth. The channels of absorption in the intestinal tract are—(1) the **capillaries** [*direct*], and (2) the **lacteals** [*indirect*] of the mucous membrane (fig. 248). Almost the whole of the substances absorbed by the former pass into the rootlets of the portal vein, and *traverse the liver*, before they reach the general circulation, while those that enter the lacteals really pass into lymphatics, so that the chyle passes through the thoracic duct and is poured by it into the blood, where the thoracic duct joins the subclavian vein (fig. 172).

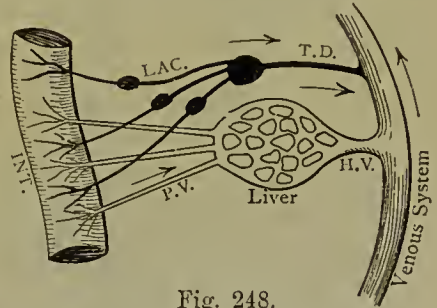


Fig. 248.

Scheme of intestinal absorption. L.A.C., lacteals; T.D., thoracic duct; P.V. and H.V. portal and hepatic veins; INT., intestine.

Watery solutions of salts, grape-sugar, peptone, poisons, and in a still higher degree alcoholic solutions of poisons, are absorbed in the **stomach**. The empty stomach absorbs more rapidly than one filled with food; gastric catarrh delays absorption. After a copious diet of milk, fatty granules have been found in the protoplasm of the goblet-cells; so that, according to this view, the goblet-cells have a double function, to secrete mucus and to absorb nutriment.

The greatest area of absorption is undoubtedly the **small intestine**, especially its *upper* half, owing to the presence of the **valvulæ conniventes** and the villi.

[Absorption takes place all along the intestine—but in the case of the fats this is strictly confined to the small intestine, where indeed all absorption is most active. We might classify the various sections of the intestinal canal, as far as regards their activity of absorption, as follows:—small intestine, large intestine, stomach, mouth, pharynx, œsophagus (*Beaunis*).]

190. STRUCTURE OF THE SMALL AND LARGE INTESTINES.—[The wall of the **small intestine** consists of four coats; which, from without inward, are named **serous**, **muscular**, **sub-mucous**, and **mucous** (fig. 249).

(1) The **serous coat** has the same structure as the peritoneum, *i.e.*, a thin basis of fibrous tissue covered on its outer surface by endothelium.

(2) The **muscular coat** consists of a thin **outer longitudinal** and an **inner thicker circular** layer of non-striped muscular fibres (fig. 249).

(3) The **sub-mucous coat** consists of loose connective-tissue containing large blood-vessels, lymphatics, and nerves, and it connects the muscular with the mucous coat.

(4) The **mucous coat** is the most internal coat, and its absorbing surface is largely increased by the presence of the **valvulæ conniventes** and villi.

[The **valvulæ conniventes** are permanent folds of the mucous membrane of the small intestine, arranged across the long axis of the gut. They pass round a half or more of the inner surface of the gut. They begin a little below the commencement of the duodenum, and are large and well marked in the duodenum, and remain so as far as the upper half of the jejunum, where they begin to become smaller, and finally disappear about the lower part of the ileum.] The **villi** are characteristic of the small intestine, and are confined to it; they occur everywhere as closely-set cylindrical projections over and between the **valvulæ conniventes** (fig. 249).

When the inner surface of the mucous membrane is examined in water, it has a velvety appearance owing to their presence. [They vary in length from $\frac{1}{50}$ to $\frac{1}{30}$ of an inch, and are largest and most numerous in the upper part of the intestine, duodenum, and jejunum, where absorption is most active, but they are less abundant in the ileum. Their total number has been calculated at four millions by Krause, and there are 10-18 on a square mm.] Each villus is a projection of the entire mucous membrane, so that it contains within itself representatives of all the tissue-

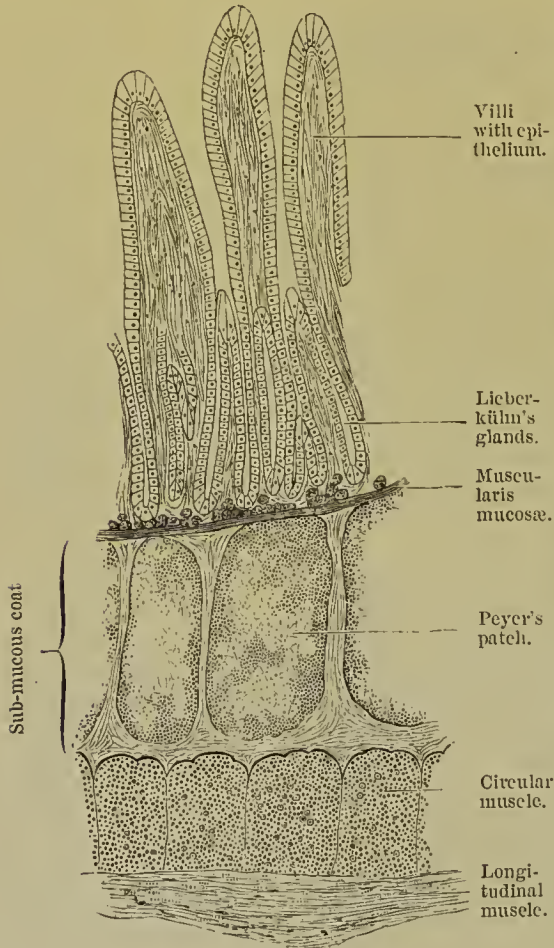


Fig. 249.

Longitudinal section through a Peyer's patch of the small intestine of a dog.

elements of the mucosa. The orifices of the glands of Lieberkühn open between the bases of villi (fig. 249).

Structure of a Villus.—Each villus, be it cylindrical or conical in shape, is covered by a single layer of **columnar epithelium**, whose protoplasm is reticulated and contains a well-defined nucleus with an intranuclear plexus of fibrils. The ends of the epithelial cells directed towards the gut are polygonal, and present the appearance of a mosaic (fig. 250, D). When looked at from the side, their free surface is seen to be covered with a clear, highly refractive **disc** or "**cuticula**," which is marked with vertical striæ. These striæ were supposed by Kölliker to represent pores for the absorption of fatty particles, but this has not been confirmed, while Brettauer and Steinach regarded them as produced by prisms placed side by side.

[According to Heidenhain, the epithelial cells are devoid of a cell wall, and their shape varies with the degree of contraction of the villus. The disc consists of rods with an intermediate substance, but they appear to be continuous with the protoplasm of the cell. Sometimes no disc is to be seen, and in this case the rods are retracted. The rods forming the disc may vary much in length. Although Heidenhain admits changes in the length of these "rods," he does not ascribe to them an active part in the absorption of fat.]

According to v. Thanhoffer, however, this clear disc is comparable to the thickened flange around the bottom of a vessel, such as is used for collecting gases. On this supposition, the upper end of each cell is open, and from it there project pseudopodia-like bundles of protoplasmic processes (fig. 250, B). These processes are supposed to be extended beyond the margin of the cell, and again rapidly retracted, and in so acting they are said to carry the fatty particles into



Fig. 250.

A, scheme of a transverse section of part of a villus; *a*, columnar epithelium with; *b*, clear disc; *c*, goblet-cell; *i*, *i*, adenoid reticulum; *d*, *d*, spaces containing leucocytes, *e*, *e*; *f*, section of the central lacteal. B, scheme of a cell with processes projected from its interior. C, columnar epithelium after the absorption of fatty granules. D, columnar epithelium of a villus seen from above with a goblet-cell in the centre.

the interior of the cells, much as the pseudopodia of an amœba entangle its food. [This view has not been confirmed by a sufficient number of observers.] Between the epithelial cells are the so-called goblet-cells (fig. 250, C). [Each goblet-cell is more or less like a chalice, narrower above and below, and broad in the middle, with a tapering fixed extremity. The outer part of these cells is filled with a clear substance or mucigen, which, on the addition of water, yields mucus. The mucigen lies in the intervals of a fine network of fibrils, which pervades the cell-protoplasm, while the protoplasm, containing a globular or triangular nucleus, is pushed into the lower part of the cell. These goblet-cells are simply altered columnar epithelial cells which secrete mucus in their interior. They are more numerous under certain conditions. Not unfrequently in a section of the mucous membrane of the gut, after it is stained with logwood, we may see a deep blue plug of mucus partly exuded from these cells. When looked at from above they give the appearance seen in fig. 250, D.] The epithelium of the villi is replaced by other cells derived from the epithelium of Lieberkühn's glands, gradually rising upwards to take the place of the shed cells. The epithelial cells are shed in enormous numbers in cholera, and in poisoning with arsenic and muscarin (*Böhm*).

[The epithelial cells covering the villus are placed upon a layer of squamous epithelium (**basement membrane**)—the sub-epithelial membrane of Débove. This basement membrane is said to be connected by processes with the so-called branched cells of the adenoid tissue of the villus, while it also sends up processes between the epithelial covering.]

The **stroma** or **body of the villus** itself consists of a basis of **adenoid tissue**, containing in its centre one or more lacteals, closely invested with several bundles of longitudinal smooth muscular fibres, derived from the *muscularis mucosæ*, and a plexus of blood-vessels. The adenoid tissue of the villus consists of a reticulum of fibrils with endothelial plates at its nodes. The spaces of the adenoid tissue form a spongy network of inter-communicating channels containing stroma-cells or leucocytes (fig. 250, A, e, e). These leucocytes or lymph-corpuscles have been seen to contain fatty granules.

[The stroma is relatively larger in amount in relation to the epithelium in the dog (fig. 259) and cat than in the rabbit and guinea-pig. In the stroma are spaces which contain leucocytes of various kinds and phagocytes. Coloration with Biondi's fluid (p. 380) enables one to single out the varieties of these cells, some of which wander out into and between the epithelial cells. The spaces also contain a coagulable fluid. The capillaries are arranged close under the epithelium (fig. 259, c).]

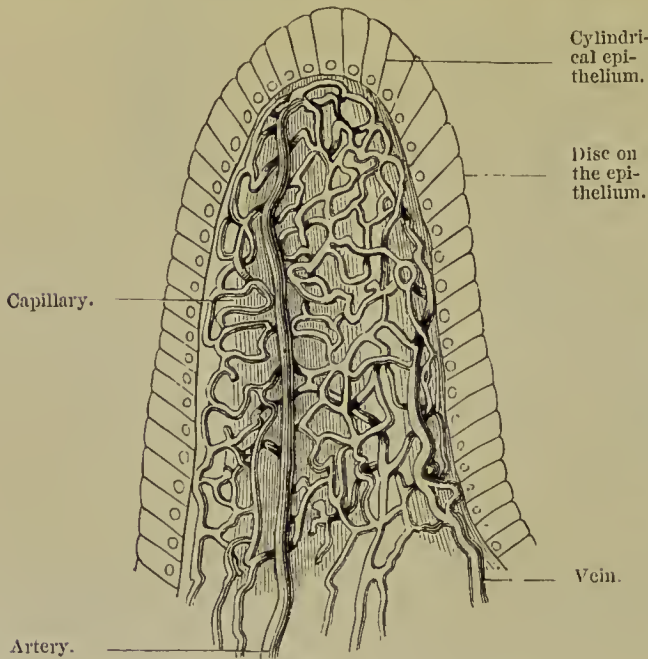


Fig. 251.

Injected blood-vessels of a villus.

from which they return towards the axis of the villus, laden with substances which they have taken into their interior (§ 192, II.). [This however is highly doubtful.]

A small **artery** placed eccentrically passes into each villus (fig. 251). In man it begins to divide about the middle of the villus, but in animals it usually runs to the apex before it divides. The capillaries resulting from the division of the artery form a fine dense network placed *superficially*, immediately under the epithelium of the surface. The blood is carried out of a villus by one or two veins (figs. 251, 252).

Non-striped muscular fibres are present in villi. They are arranged longitudinally in several bundles from base to apex immediately outside the central lacteal.

The **lymphatic** or **lacteal** lies in the axis of the villus (fig. 252, d). Some regard the lacteal merely as a space in the centre of the villus, but more probably it has a distinct wall composed of endothelial cells, with apertures or stomata here and there between the cell-plates. These stomata place the interior of the lacteal in direct communication with the spaces of the adenoid tissue. Perhaps white blood-corpuscles wander out of the blood-vessels of the villi into the spaces of the adenoid tissue, where they become loaded with fatty granules, and pass into the central lacteal. Zuwarykin and Wiedersheim suppose that the leucocytes pass from the parenchyma of the villus towards the epithelial layer, and even between the epithelial cells,

[Each bundle is surrounded by a connective-tissue sheath.] When they contract they tend to empty the lacteal. A few muscular fibres are placed more superficially and run in a more transverse direction. [The longitudinal bundles of non-striped muscle in the villi are connected together by oblique strands; while the longitudinal bundles shorten the villus, the oblique fibres keep the lacteal open; thus the parenchyma of the villus is also compressed transversely, whereby the products of absorption are forced into the lacteal. The muscles are fixed by cement to the sub-epithelial basal membrane. The muscular fibres of the villi are direct prolongations of the muscularis mucosæ.]

Nerves pass into the villi from Meissner's plexus lying in the sub-mucous coat. The nerves to the villi are said to have small granular ganglionic cells in their course, and they terminate partly in the muscular fibres and partly in the arteries of the villi.

On making a vertical section of the mucous membrane of the small intestine one sees the villi, and under them a network of adenoid tissue loaded with leucocytes. This tissue forms its basis, and in it are placed vertically side by side, like test-tubes in a stand, immense numbers of simple tubular glands—the **crypts** or **glands of Lieberkühn** (fig. 249). [Kultschitzki finds that the connective-tissue framework of the mucous membrane of the small intestine is not true adenoid tissue, but a transition form between the latter and loose fibrous tissue.] **Lieberkühn's glands** open above at the bases of the villi, while their closed lower extremity reaches almost to the muscularis mucosæ.

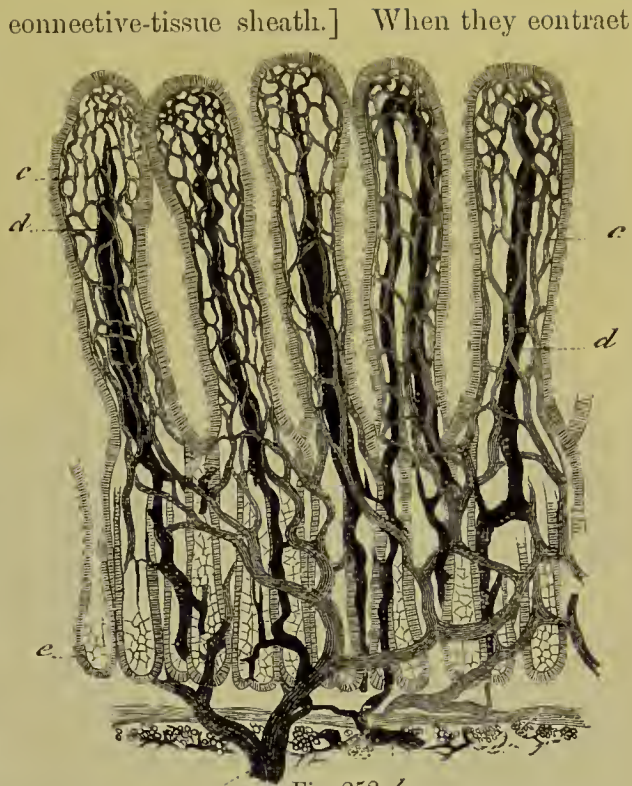


Fig. 252

Mucous membrane of the small intestine of the dog; the lacteals are black, and the blood-vessels lighter. *a*, artery; *b*, lymphatic; *c*, plexus of capillaries in the villi; *d*, lacteal; *e*, Lieberkühn's glands.

Villi with blood-vessels injected. Solitary follicle.

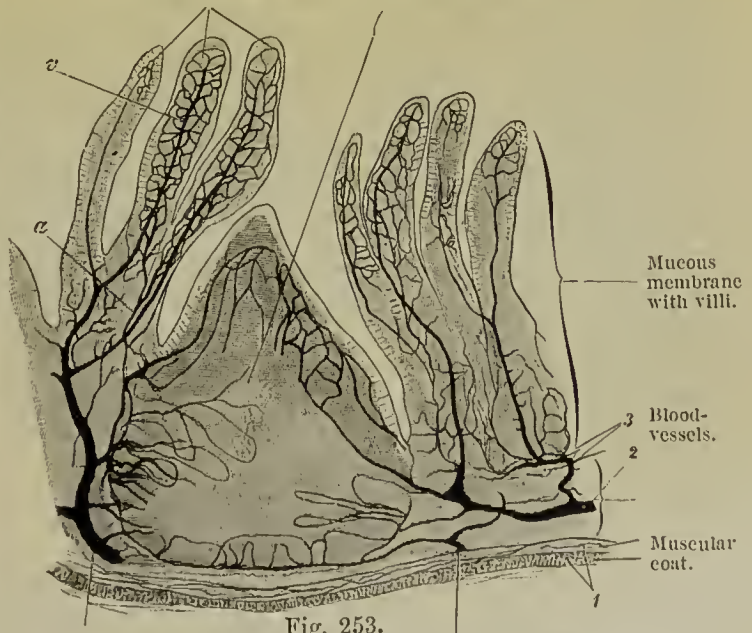


Fig. 253.

Transverse section of duodenum of a rabbit injected, $\times 50$.

Each tube consists of a basement membrane lined by a single layer of columnar epithelium, leaving a wide lumen, the cells lining them being continuous with those that cover the mucous membrane. Many of the cells exhibit mitotic figures, *i.e.*, they are about to divide. Some goblet-cells are often found between the columnar epithelium.



Fig. 254.

Section of a solitary follicle of the small intestine (human). *a*, lymph-follicle covered with epithelium (*b*); but the villi, *c*, are denuded of epithelium; *d*, Lieberkühn's follicle; *e*, muscularis mucosae; *f*, sub-mucous tissue.

[Brunner's glands are compound tubular glands lying in and confined to the sub-mucous coat of the duodenum (figs. 214, 238). Their ducts perforate the muscularis mucosae to open

on the surface. They seem to be the homologues of the pyloric glands of the stomach (fig. 214).]



Fig. 255.

Diagram of a vertical section of the mucous membrane of the small intestine of a dog, showing the closed follicles. *aa*, part of a Peyer's patch; *b*, muscularis mucosae.

[Solitary Follicles are small round or oval white masses of adenoid tissue ($\cdot 5$ –2 mm. in diameter), with their deeper parts embedded in the submucosa, and their apices projecting into the mucosa of the intestine. They begin at the pyloric end of the stomach, and are found throughout the whole intestine—small and large.

They consist of small masses of adenoid tissue loaded with leucocytes (fig. 254). The

small, round, or oval masses at first lie in the mucous coat, their apex covered by the epithelium, with few goblet-cells, while their outer part rests on the muscularis mucosæ. As they develop, they grow outwards through the muscularis mucosæ, and penetrate into the sub-mucous coat, so that they become pear-shaped, the narrow end of the pear being directed towards and covered by the epithelium of the gut. At the same time Lieberkühn's glands are pressed aside and no villi lie over the follicles. In the centre of each is a germ-centre, where the leucocytes often exhibit mitosis. Many of the leucocytes wander out between the epithelial cells just as in the tonsil. They are well supplied with blood-vessels (§ 197), although no lymphatic vessels enter them. They are surrounded by lymphatics, and, in fact, they may be said to hang into a lymph-stream. The

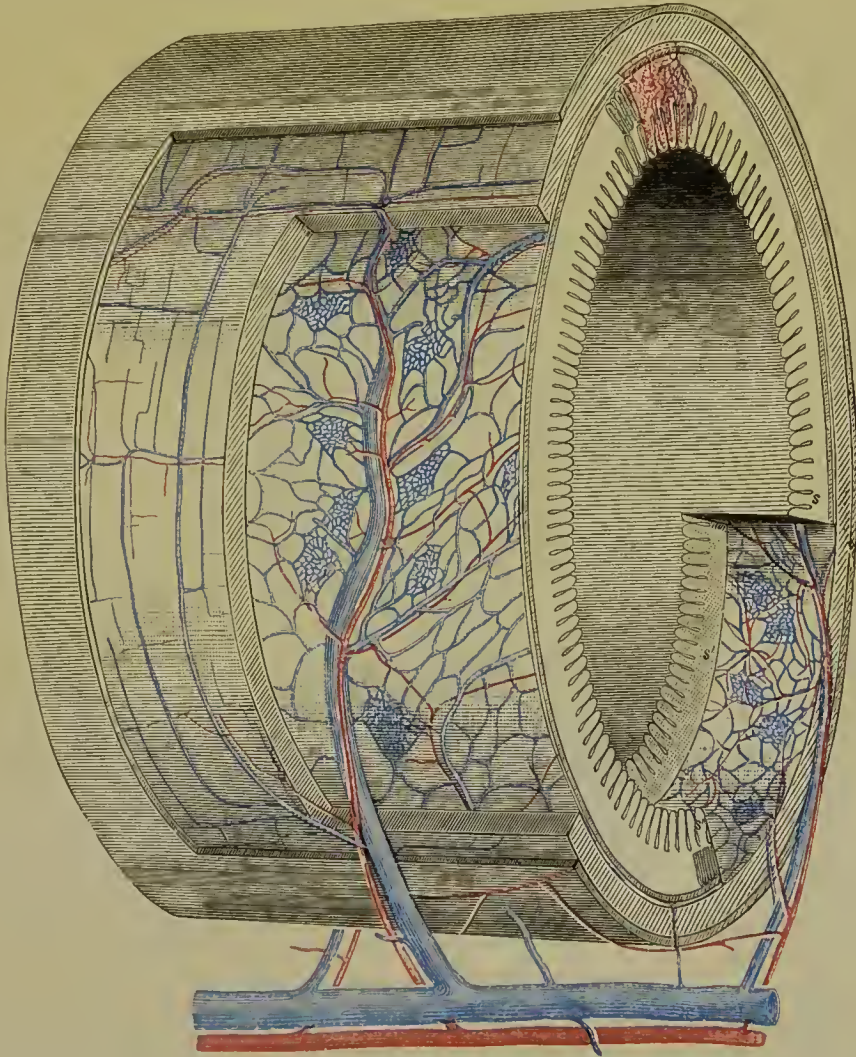


Fig. 256.

Scheme of the blood-vessels of the small intestine. Arteries red, veins blue. The various coats are shown schematically. *s*, villi.

distribution of solitary follicles is fairly uniform in the small intestine; their number generally increases from the stomach to the large intestine; although there are considerable variations in different individuals, there seems to be the same number of solitary follicles and Peyer's patches in the infant as in the adult.

[Peyer's patches, or agminated glands, consist of groups (10-80 or more)

of lymph-follicles, lying side by side like the foregoing (figs. 249, 255). The masses are often more or less fused together, their bases lie in the sub-mucosa, while their summits project into the mucosa, where they are covered merely by the columnar epithelium of the intestine. The lymph-corpuses often pass between the epithelial cells. The patches so formed have their long axis in the axis of the intestine, and they are always placed opposite the attachment of the mesentery. Like the solitary glands, they are well supplied with blood-vessels, while around them is a dense plexus of lymphatics or lacteals. They are most abundant in the lower part of the ileum. These glands are specially affected in typhoid fever.]

[**Blood-vessels of the small intestine** (fig. 256).—Branches of the mesenteric arteries from between the two layers of the peritoneum reach the intestine, and ramify under the serous coat. At intervals they penetrate the longitudinal and circular muscular coats, giving off branches of supply to these as they pass. Fairly large branches enter the sub-mucous coat and ramify in it, and from these fine

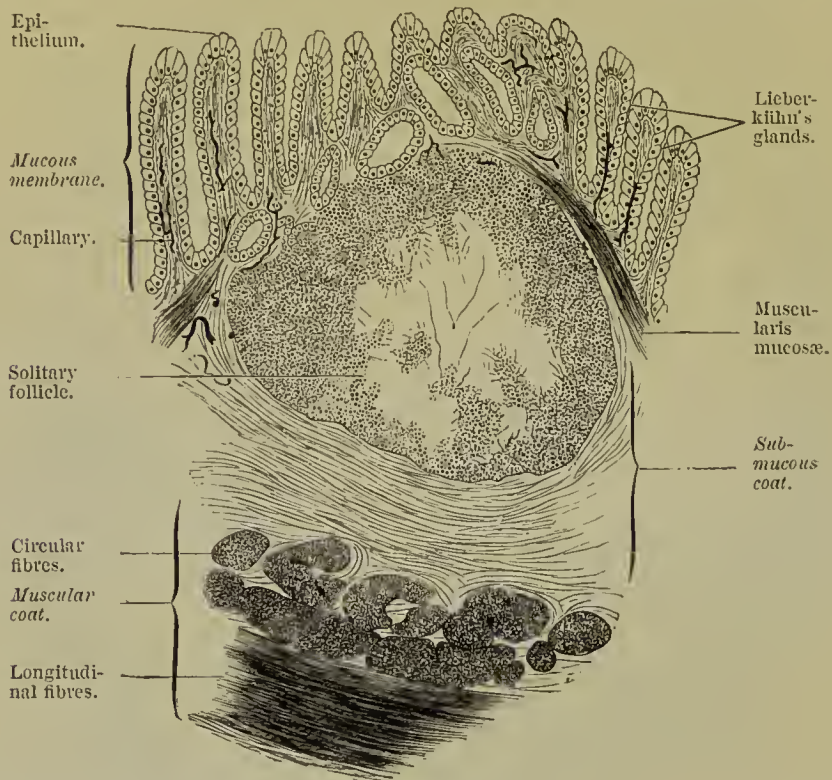


Fig. 257.

Longitudinal section of the large intestine.

branches arise, which run vertically, and form a rich plexus around Lieberkühn's glands, while another branch ascends in each villus as already described. The blood is returned by corresponding veins. Mall has shown that small capillary venous plexuses exist in the sub-mucous coat. The mucous coat is far more vascular than the muscular.]

[**Nerves of the intestine.**—The nerves of the **small intestine** come from the superior mesenteric plexus, and pass along the branches of the superior mesenteric artery. The **large intestine** is supplied by branches from the inferior mesenteric and hypogastric plexuses. The, for the most part, non-medullated nerve-fibres pass from the vessels to the intestine, where they form a plexus under the peri-

toneal coat of the gut and from this branches penetrate the muscular coat to form **Auerbach's plexus**. This plexus exists throughout the whole intestinal tract, lying between the longitudinal and circular muscular coats (figs. 205, 206). This plexus, with angular or polygonal meshes, consists of non-medullated nerves with groups of multipolar ganglionic cells at the nodes. Fibres are given off by it to the muscular coats. Connected by branches with the foregoing, and lying in the sub-mucosa, is the **plexus of Meissner**, which is much finer, the meshes being wider, the nodes smaller, but also provided with ganglionic cells. It supplies the muscular fibres and arteries of the mucosa, including those of the villi. It also sends branches to Lieberkühn's glands (fig. 207).]

[**Structure of the Large Intestine.**—It has four coats, like those of the small intestine. The **serous coat** has the same structure as that of the small intestine. The **muscular coat** has external *longitudinal* fibres occurring all round the gut, but they form three flat ribbon-like longitudinal bands in the cæcum and colon (fig. 257). Inside this coat are the *circular* fibres. The **sub-mucosa** is practically the same as that of the small intestine. The **mucosa** is distinguished by negative characters. It has no villi and no Peyer's patches, but otherwise it resembles structurally the small intestine, consisting of a basis of adenoid tissue with the simple tubular **glands of Lieberkühn** (fig. 239). These glands are very numerous and somewhat longer than those of the small intestine, and they always contain far more goblet-cells—about ten times as many. The cells lining them are devoid of a clear disc. **Solitary glands** occur throughout the entire length of the large intestine. At the bases of Lieberkühn's glands is the **muscularis mucosæ**. The **blood-vessels** and nerves have a similar arrangement to those in the stomach.]

[**Blood-Vessels.**—On looking down on an opaque injection of the mucous membrane of the stomach, one sees a dense meshwork of polygonal areas of unequal size, with depressions here and there. The orifices are the orifices of the gastric glands, each surrounded by a capillary. A somewhat similar appearance is seen in an opaque injection of the mucous membrane of the large intestine, but in the latter the meshwork is *uniform*, all the orifices (of Lieberkühn's glands) being of the same size.]

191. ABSORPTION OF THE DIGESTED FOOD.—The physical forces concerned are :—**endosmosis, diffusion, and filtration.**

All the constituents of the food, with the exception of the fats, which in part are changed into a fine emulsion, are brought into a state of **solution** by the digestive processes. These substances pass through the walls of the intestinal tract, either into the blood-vessels of the mucous membrane or into the beginning of the lymphatics. In this passage of the fluids two physical processes come into play—*endosmosis* and *diffusion* as well as *filtration*.

I. Endosmosis and diffusion occur between two fluids which are capable of forming an intimate mixture with each other, *e.g.*, hydrochloric acid and water, but never between two fluids which do not form a perfect mixture, such as oil and water. If two fluids capable of mixing with each other, but of different compositions, be separated from each other by means of a **septum** with physical pores (which occur even in a homogenous membrane), an exchange of the constituents in the fluids occurs until both fluids have the same composition. This exchange of fluids is termed *endosmosis* or *diosmosis*.

Diffusion.—If the two miscible fluids are placed in a vessel, the one fluid over the other, but without being separated by a porous septum, an exchange of the particles of the fluids also occurs, until the whole mixture is of uniform composition. This process is called *liquid diffusion*.

Conditions influencing Diffusion.—Graham's investigations showed that the rapidity of diffusion is influenced by—(1) The nature of the fluids themselves; acids diffuse most rapidly; the alkaline salts more slowly; and most slowly, fluid albumin, gelatin, gum, dextrin. These last do not crystallise, and perhaps do not form true solutions. (2) The more concentrated the solutions, the greater the diffusion. (3) Heat accelerates, while cold retards, the process. (4) If a solution of a body which diffuses with difficulty be mixed with an easily diffusible one, the former diffuses with still greater difficulty. (5) Dilute solutions of several substances diffuse into each other without any difficulty, but if concentrated solutions are employed, the process is retarded. (6) Double salts, one constituent of which diffuses more readily than the other, may be chemically separated by diffusion.

Endosmometer.—The exchange of the fluid-particles takes place independently of the

hydrostatic pressure. An endosmometer (fig. 258) consists of a glass cylinder filled with distilled water, and into this is placed a flask, J, without a bottom, instead of which a membrane, *m*, is tied on. A glass tube, R, is fixed firmly by means of a cork into the neck of the flask. The flask is filled up to the lower end of the tube with a concentrated salt solution, and is then placed in the cylindrical vessel until both fluids are on the same level, *x*. The fluid in the tube, R, soon begins to rise, because water passes through the membrane into the concentrated solution in the flask, and this independently of the hydrostatic pressure. Particles of the concentrated salt solution pass into the cylinder and mix with the water, F. These outgoing and ingoing currents continue until the fluids without and within J are of uniform composition, whereby the fluid in R always stands higher (*e.g.*, at *y*), while it is lowered in the cylinder. The circumstance of the level of the fluid within the tube being so high, and remaining so, is due to the fact that the pores in the membrane are too fine to allow the hydrostatic pressure to act through them.

Endosmotic Equivalent.—Experiment has shown that equal weights of different soluble substances attract different amounts of distilled water through the membrane, *i.e.*, a known weight of a soluble substance (in the flask) can be exchanged by endosmosis for a definite weight of water. The term “endosmotic equivalent” indicates the weight of distilled water that passes into the flask of the endosmometer, in exchange for a known weight of the soluble substance (*Jolly*). For 1 gm. alcohol 4.2 grms. water were exchanged; while for 1 gm. NaCl, 4.3 grms. water passed into the endosmometer. The following numbers give the endosmotic equivalent of

Acid potassium sulphate, = 2.3	Magnesium sulphate, = 11.7
Common Salt, . . = 4.3	Potassium sulphate, . = 12.0
Sugar, . . . = 7.1	Sulphuric acid, . = 0.39
Sodium sulphate, . . = 11.6	Potassium hydrate, . = 215.0

The amount of the substance which passes through the membrane into the water of the cylinder is proportional to the concentration of the solution. If the water in the cylinder, therefore, be repeatedly renewed, the endosmosis takes place more rapidly and the process of equilibration is accelerated. The larger the pores of the membrane, and the smaller the molecules of the substance in solution, the more rapid is the endosmosis. Hence, the rapidity of endosmosis of different substances varies, *e.g.*, the rapidity of sugar, sodium sulphate, common salt, and urea is in the ratio of 1 : 1.1 : 5 : 9.5.

The endosmotic equivalent is not constant for each substance. It is influenced by—(1) The temperature, which, as it increases, generally increases the endosmotic equivalent. (2) It also varies with the degree of concentration of the osmotic solutions, being greater for dilute solutions of the substances.

If a substance other than water be placed in the cylinder, an endosmotic current occurs on both sides until complete equality is obtained. In this case, the currents in opposite directions disturb each other. If two substances be dissolved in the water in the flask at the same time, they diffuse into water without affecting each other. (3) It also varies with membranes of varying porosity. Common salt, which gives an endosmotic equivalent with a pig's bladder = 4.3 gives 6.4 when an ox bladder is used; 2.9 with

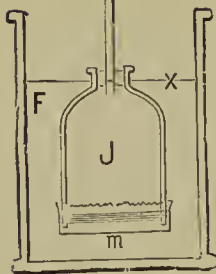


Fig. 258.

Endosmometer.

a swimming bladder; and 20.2 with a collodion membrane.

Colloids.—There are many fluid-substances which, on account of the great size of their molecules, do not pass, or pass only with difficulty, through the pores of a membrane impregnated with gelatinous bodies, which diffuse slowly. These substances are not actually in a true state of solution, but exist in a very dilute condition of imbibition. Such substances are the fluid proteids, starches, dextrin, gum, and gelatin. These diffuse when no septum is present, but diffuse with difficulty or not at all through a porous septum. Graham called these substances **colloids**, because, when concentrated, they present a gluc-like or gelatinous appearance; further they do not crystallise, while those substances which diffuse readily are crystalline, and are called **crystalloids**. Crystallisable substances may be separated from non-crystallisable by this process, which Graham called **dialysis**. Mineral salts favour the passage of colloids through membranes.

That **endosmosis** and **diffusion** take place in the intestinal tract, through the mucous membrane and the delicate membranes of the blood- and lymph-capillaries, cannot be denied. On the one side of the membrane, within the intestine, are relatively concentrated solutions of highly diffusible salts, peptones, sugar, and soaps, and within the blood-vessels are the colloids, which are scarcely diffusible, *e.g.*, the proteids of blood and lymph.

II. Filtration is the passage of fluids through the **coarse** intermolecular pores of a membrane owing to pressure. The greater the pressure, and the larger and more numerous the pores, the more rapidly does the fluid pass through the membrane; increase of temperature also accelerates it. Those substances which are imbibed by the membrane filter most rapidly, so that the same substance filters through different membranes with varying rapidity. The filtration is usually slower, the greater the concentration of the fluid. The filter has the property of retaining some of the substances from the solution passing through it, *e.g.*, colloid substances—or water (in dilute solutions of nitre). In the former case, the filtrate is more dilute, in the latter more concentrated, than before filtration. Other substances filter without undergoing any change of concentration. Many membranes behave differently, according to which surface is placed next the fluid; thus the shell-membrane of an egg permits filtration only from without inwards; [and the same is true to a much less extent with filter-paper; the smooth side of the filter-paper ought always to be placed next the fluid to be filtered. The intact skin of the grape prevents the entrance of fungi into the fruit.] There is a similar difference with the gastric and intestinal mucous membrane.

[By using numerous layers of filter-paper, many colloids and crystalloids are retained in the filter, *e.g.*, hemoglobin, albumin, and many colouring matters, especially aniline colours, the last being arrested by glass-wool (*Krysinski*).]

[Filtration of Albumin.]—Runeberg finds that the amount of albumin in pathological transudations varies with (1) the *capillary area*, being least in œdema of the subcutaneous tissue. (2) The presence or absence of *inflammatory processes* in the vascular wall, non-inflammatory pleuritic effusion containing 2 per cent., and inflammatory 6 per cent., of albumin. (3) The condition and amount of *albumin in the blood*. The amount of albumin in the transudate never reaches, although it sometimes approaches, that in blood. In ascites in general dropsy the amount is .03 to .04 per cent. (4) The *duration* of the transudation. (5) Perhaps the blood-pressure and the condition of the circulation.]

Filtration of the soluble substance may take place from the canal of the digestive tract when :—(1) The *intestine contracts* and thus exerts pressure upon its contents. This is possible when the tube is narrowed at two points, and the musculature between these two points contracts upon the fluid-contents. (2) Filtration, under **negative pressure**, may be caused by the **villi** (*Brücke*). When the villi contract energetically, they empty their contents towards the blood- and lymph-vessels. The lacteal remains empty, as the chyle is prevented from passing backwards into the origin of the lacteal within the villi, owing to the presence of numerous valves in the lymphatics. When the villi relax, they are refilled with fluids from the intestine.

192. ABSORPTION BY THE INTESTINAL WALL.—I. True solutions undoubtedly pass by endosmosis into the blood-vessels and lymphatics of the intestinal walls, but numerous facts indicate that the protoplasm of the cells takes an active part in the process of absorption. The forces concerned have not as yet been proved to be purely physical and chemical in their nature.

(1) **Inorganic Substances.**—**Water** and the **soluble salts** necessary for nutrition are easily absorbed, the latter especially by the **blood- and lymph-vessels**. When saline solutions pass by endosmosis into the vessels, water must pass from the intestinal vessels into the intestine. The amount of water, however, is small, owing to the small endosmotic equivalent of the salts to be absorbed. More salts are absorbed from concentrated than from dilute solutions. If large quantities of salt, with a high endosmotic equivalent, *e.g.*, magnesium or sodium sulphate, are introduced into the intestine, these salts retain the water necessary for their solution, and may thus cause diarrhœa. Conversely, when these substances are injected into the blood, a large quantity of water passes from the intestine into the blood, so that constipation occurs, owing to dryness of the intestinal contents (*Aubert*).

[M. Hay concludes from his experiments (§ 161) that salts, when placed in the intestines, do not abstract water from the blood, or are themselves absorbed, in virtue of an endosmotic relation being established between the blood and the saline solution in the intestines. Absorption is probably due to the filtration and diffusion, or processes of imbibition other than endosmosis, as yet little understood. The result obtained by Aubert, which is not constant, is mostly caused by the great diuresis which the injected salt excites.] The absorption of fluids takes place best at a medium pressure of 80 to 140 cm. of water within the intestine; higher pressure

compresses the blood-vessels and diminishes the absorption. During digestion, owing to the dilatation of the vessels, absorption is more rapid. The fact that 0.5 per cent. solution of NaCl is absorbed better than water, and soda solution than potash solution, seems to show that physical forces are not the only factors concerned.

Numerous inorganic substances, which do not occur in the body, are absorbed by endosmosis from the intestine, *e.g.*, dilute sulphuric acid, potassium iodide, chlorate, and bromide, and many other salts.

[That the water passes chiefly into the blood-capillaries, and only a small amount by the lacteals, appears to be due to the superficial position of these capillaries immediately under the epithelium of the villus (fig. 259, *c.*). If water be injected

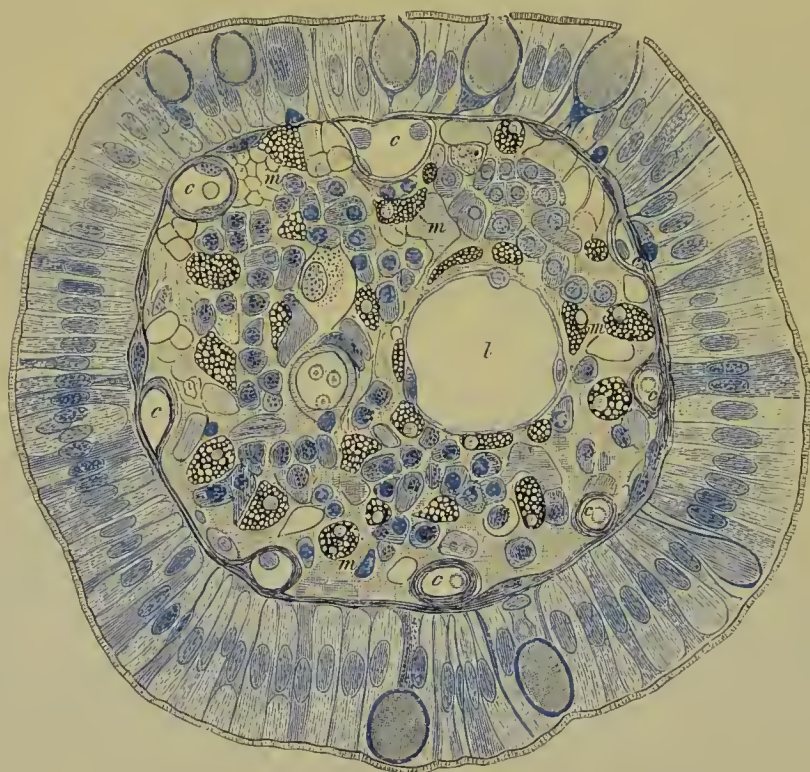


Fig. 259.

Transverse section of an intestinal villus (dog). *l*, lacteal ; *c*, capillaries ; *m*, muscular fibres.

into a loop of intestine in the dog, and a fistula made on the thoracic duct so as to collect the chyle, the chyle-stream is but slightly increased during the absorption of the water from the intestine, so that perhaps a large part of the fluid of the chyle is derived from the lymph formed by the capillaries of the villi. The water appears to pass between the cells, as well as through, the cell protoplasm.

Physical forces, *e.g.*, diffusion, do not seem to yield a satisfactory explanation of the absorption of water from the intestine. If a solution of grape-sugar and sodic sulphate be injected into a loop of intestine, the whole of the former is absorbed, but there always remains a considerable amount of the latter in the gut, although sodic sulphate has a higher rate of diffusion than grape-sugar. Indeed, for many soluble substances (*e.g.*, pigments) the epithelium is quite impervious.

As a general rule, soluble substances pass in the same way as the water, *i.e.*, into the blood-vessels.]

(2) The **soluble carbohydrates**, such as the **sugars**, of which the chief representatives are **maltose** and **dextrose**, with a relatively high endosmotic equivalent.

Cane-sugar is changed by a special ferment into invert-sugar (§ 183, 5). Absorption appears to take place somewhat slowly, as only very small quantities of grape-sugar are found in the chyle vessels, or the portal vein, at any time. According to v. Mering, the **sugar** passes from the intestine into the **rootlets of the portal vein**; dextrin is also said to occur in the portal vein. [This latter statement is highly doubtful.] When the blood of the portal vein is boiled with dilute sulphuric acid the amount of sugar is increased. [There is no proof that the carbohydrates are absorbed in any other form than sugar.] The amount of sugar absorbed depends upon the concentration of its solution in the intestine; hence the amount of sugar in the blood is increased after a diet containing much of this substance, so that it may appear in the urine; in which case the blood must contain at least 0.6 per cent. of sugar. A small amount of **cane-sugar** has also been found in the blood (*Cl. Bernard*). If a large quantity of sugar be present in the intestine a part passes into the lymphatics or lacteal (*Ginsberg*). The sugar is used up in the bodily metabolism; some of it is perhaps oxidised in the muscles (§ 176).

[**Injection of sugar into blood.**—Lactose when injected into a vein is excreted unchanged in the urine, but galactose is almost completely assimilated, only a trace appearing in the urine. Lactose, therefore, requires to be changed in the intestinal canal before it can be assimilated (*Dastre*). **Cane-sugar** is excreted in the urine as a foreign body. **Grape-sugar** (p. 324).]

(3) The **peptones** have a small endosmotic equivalent, a 2 to 9 per cent. solution = 7 to 10 [while albumin has 100]. Owing to their great **diffusibility** they are readily absorbed, and they are the chief representatives of the proteids which are absorbed. The amount absorbed depends upon the concentration of their solution in the intestine. [According to Plósz and Györgyai, Drosdoff and Schmidt-Mulheim, peptones occur only in traces in the blood of the portal vein. Neumeister, however, using the best methods, finds that although peptones are abundant in the intestine, not a trace of peptone or of the albumoses is found either in the blood or lymph. This coincides with Hofmeister's researches. As no peptones or albumoses have been found in the blood, and as they can compensate for the total metabolism of the proteids within the body, we must assume that they are rapidly converted into true albuminous bodies, somewhere between the cavity of the intestine and the blood-stream, *i.e.*, in the wall of the intestine itself.] Hofmeister supposes that the leucocytes absorb the peptones and act as their carriers, much as the red corpuscles are oxygen carriers. They carry the peptones into the mucous membrane of the stomach and small intestine, which are very rich in peptone at the fourth hour of digestion. [The number of leucocytes is greatly increased in the mucous membrane, especially in the stomach and upper part of the duodenum, during digestion, and diminished during fasting in dogs and cats. The same is the case with the lymph-follicles, the cells of which are formed by the division of the pre-existing cells. [Thus the mucous membrane possesses the property of *changing peptone into albumin* (*Salvioli*). Heidenhain regards the epithelium of the villi as the seat of these changes. He supposes that the epithelium covering the villi reconvert the peptone into albumin, and give it up to the blood-capillaries lying immediately below the epithelial cells. At all events, some structures in the mucous membrane are capable of effecting the reversion of peptones into albumin.] When animals are fed on peptones (with the necessary fat or sugar), these serve to maintain the body-weight.

[It was formerly stated that the liver possessed the power of converting peptones into albumin. Neumeister completely disproved this view by perfusing blood containing peptones through an excised but still living liver, and finding that no such change was effected. Also by injecting peptones and albumoses into a mesenteric vein, almost all the peptone was excreted by the urine, only a minute quantity being found in the small intestine.]

[If a loop of mesentery be excised, and blood perfused through its arteries, *i.e.*, an artificial circulation kept up, the loop will live for some time. If peptone be placed in the cavity of the loop, it will gradually disappear from the intestine, nor can it be recovered from the blood.

It is absorbed, but apparently not as peptone. It is not changed by the blood, for peptone added to blood before it is perfused can be recovered from the blood after its perfusion. This experiment also points to the peptone being changed in its passage through the wall of the intestine (*Ludwig and Salviole*).]

[**Injection of Peptone into Blood.**—When peptone is slowly injected into the blood of an animal, within a short time thereafter no trace of the peptone is to be found in the blood, liver, spleen, or small intestine, and only traces in the kidney. It is rapidly excreted, by the kidneys, so that the urine is like a solution of peptone. If a large quantity be rapidly injected the rabbit dies, and much peptone is found in the small intestine. It would seem as if the kidneys could not excrete it quick enough, with the result that it passed into the intestine. Peptones, or rather albumoses, so injected prevent the blood of the dog (not of the rabbit, cat, or pig) from coagulating (p. 36). In large quantity they are fatal. Five cc. of a 20 percent. solution in 0.6 percent. NaCl solution is fatal to a dog weighing about 8 kilos. (17 lbs.). The peptones used in these experiments were really a mixture of peptones and albumoses. Neumeister finds that in the dog, when albumoses are injected into the blood they reappear in the urine, but somewhere in the body they undergo hydration in the sense in which peptic digestion causes hydration. The two primary albumoses reappear almost completely as deutero-albumose, and deutero-albumose, when introduced, reappears as peptone. Peptone, however, reappears unchanged. In rabbits, albumose reappears unchanged in the urine.]

(4) **Unchanged true proteids** filter with great difficulty, and much albumin remains upon the filter. On account of their high endosmotic equivalent they pass with extreme slowness, and only in traces, through membranes. Nevertheless, it has been conclusively proved that unchanged proteids can be absorbed (*Brücke*), e.g., casein, soluble myosin, alkali-albuminate, albumin mixed with common salt, gelatin (*Voit, Bauer, Eichhorst*). They are absorbed even from the large intestine (*Czerny and Latschenberger*), although the human large intestine cannot absorb more than 6 grms. daily. But the amount of unchanged proteids absorbed is always very much less than the amount of peptone.

Other proteids.—Egg albumin without common salt, syntonin, serum-albumin, and fibrin are not absorbed from the intestine (*Eichhorst*). Landois observed, in the case of a young man who took the whites of 14 to 20 eggs along with NaCl, that albumin was given off by the urine for 4 to 10 hours thereafter. The amount of albumin given off rose until the third day, and ceased on the fifth day. The more albumin taken, the sooner the albuminuria appeared, and the longer it lasted. The unchanged egg-albumin reappeared in the urine. If unboiled egg-albumin be injected into the blood, part of it reappears in the urine, [so that it is not assimilated by the tissues. Before this can occur it must be altered in the digestive tract. If it be changed into syntonin or into alkali albumin, however, and then injected into a vein (dog), not a trace of these appears in the urine, so that they seem to be assimilated in the blood-stream. Casein similarly injected causes albuminuria, so that the changes casein undergoes during digestion prevents it from being excreted from the blood by the kidneys (*Neumeister*) (§ 41, 2), (*Stokvis, Lehmann*).]

(5) The soluble **fat-soaps** represent only a fraction of the fats of the food which are absorbed; the greater part of the neutral fats being absorbed in the form of very fine particles—as an emulsion (§ 192, II.). The *absorbed soaps have been found in the chyle*, and as the blood of the portal vein contains more soaps during digestion than during hunger, it has been assumed that the soaps pass into the intestinal blood-capillaries. Still only a very small amount passes into the blood (*J. Munk*).

The investigations of Lenz, Bidder, and Schmidt render it probable that the organism can absorb only a limited amount of fat within a given period; the amount, perhaps, bears a relation to the amount of bile and pancreatic juice. The maximum per kilo. (cat) was 0.6 gm. of fat per hour.

[**Injection of soaps into the blood.**—If a certain amount of pure oleate of soda (soap) per kilogram weight be injected into a vein in a dog or rabbit, the blood-pressure falls and death may take place. If, however, the soap solution be injected into the rootlets of the portal vein it requires much more soap, so that the liver appears to retain a large part of it, or change it chemically. If volatile fatty acids (butyrate of soda) be injected instead, about ten times the amount can be injected. Injection of soaps into the blood retards the coagulation of the blood. In some respects, therefore, soap-injection is like peptone-injection, but the poisonous action of the peptone is not diminished by the liver as is the case with the soaps.]

The greatest amount of the fats in the intestine are conveyed to the chyle as **neutral fats**. It would appear that the soaps reunite with glycerin in the paren-

ehyma of the villi, to form neutral fats, as Perewoznikoff and Will found neutral fats, after injecting these two ingredients into the intestinal canal, while Ewald found that fat was formed when soaps and glycerin were brought into contact with the living fresh intestinal mucous membrane. No **fatty acids** are found in blood (§ 32, II.) or chyle (§ 198).

Absorption of other Substances.—Of soluble substances which are introduced into the intestinal canal, some are absorbed and others are not. The following are absorbed:—alcohol, part of which appears in the urine (not in the expired air), viz., that part which is not changed into CO_2 and H_2O , within the body; tartaric, citric, malic, and lactic acids; glycerin, inulin; gum and vegetable mucin, which give rise to the formation of glycogen in the liver.

Amongst **colouring matters**, alizarin (from madder), alkanat, indigo-sulphuric acid, and its soda-salt are absorbed; hæmatin is partly absorbed, while chlorophyll is not. **Metallic salts** seem to be kept in solution by proteids, are perhaps absorbed along with them, and are partly carried by the blood of the portal vein to the liver (ferric sulphate has been found in chyle). Numerous **poisons** are very rapidly absorbed, e.g., hydrocyanic acid after a few seconds; potassium cyanide has been found in the chyle. [If salts (Kl, sulphocyanide of ammonium) be injected into a ligatured loop of intestine (dog, cat, rabbit), these substances are absorbed both by the blood- and lymph-vessels, and in both nearly simultaneously.]

Even for the absorption of completely fluid substances, endosmosis and filtration seem to be scarcely sufficient. An active participation of the protoplasm of the cells seems here also—in part at least—to be necessary, else it is difficult to explain how very slight disturbances in the activity of these cells, e.g., from intestinal catarrh, cause sudden variations of absorption, and even the passage of fluids into the intestine.

If absorption were due to effusion alone, when alcohol is injected into the intestine, water ought to pass into the intestine, but this does not occur. Brigger found that the injection of a 0.5 to 1 per cent. solution of salts into a ligatured loop of intestine did not cause water to pass into the intestine; but it appeared when a 20 per cent. solution was injected.

II. Absorption of the Smallest Particles.—The largest amount of the **neutral fats** and also the **fatty acids** are simultaneously absorbed in the form of a milk-like **emulsion**, formed by the action of the bile and the pancreatic juice, and consisting of excessively small granules of uniform size (§ 170, III.; § 181). The fats themselves are not chemically changed, but remain as undecomposed neutral fats. The particles seem to be surrounded by a delicate albuminous envelope, or haptogen membrane, partly derived from the pancreatic juice [probably from its alkali-albuminate.] The process of the absorption of fat by the villi is one of the most obscure in physiology. The **villi** of the small intestine are the chief organs concerned in the absorption of the fatty emulsion, but the epithelium of the stomach and that of the large intestine also take a part. The fatty granules are recognised in the villi—(1) Within the delicate canals? (§ 190), in the clear band of the epithelium (*Köliker*). [It is highly doubtful if the vertical lines seen in the clear disc of the epithelium of the intestine are due to pores.] (2) The protoplasm of the epithelial cells is loaded with fatty granules of various sizes during the time of absorption, while the nuclei of the cells remain free, although, from the amount of fat within the cells, it is often difficult to distinguish them (fig. 260). (3) The granules pass into the spaces of the parenchyma of the villi; these spaces communicate freely with each other. (4) The origin of the **central lymphatic** or **lacteal** in the axis of the villus is found to be filled with fatty granules.

The **amount of fat** in the chyle of a dog, after a fatty meal, is 8 to 10 per cent., while the fat disappears from the blood within thirty hours.

[**Absorption of fat.**—1. **Within the epithelial cells.**—As to the absorption of fats, the balance of evidence goes to show that it passes through the **body of the epithelial cells**, but what forces are concerned in this process is not certain. The bile at least seems to aid the process within the epithelial cells; the fat appears in droplets of variable size (fig. 260). The fat enters in small droplets, which in the protoplasm of the cell may run together to form larger ones. The fatty contents seem to be driven out of the body of the cells by the contraction of the protoplasm of the cells.

2. In the spaces of the stroma of the villi.—The fatty granules then pass into the pericellular spaces of the stroma of the villi.

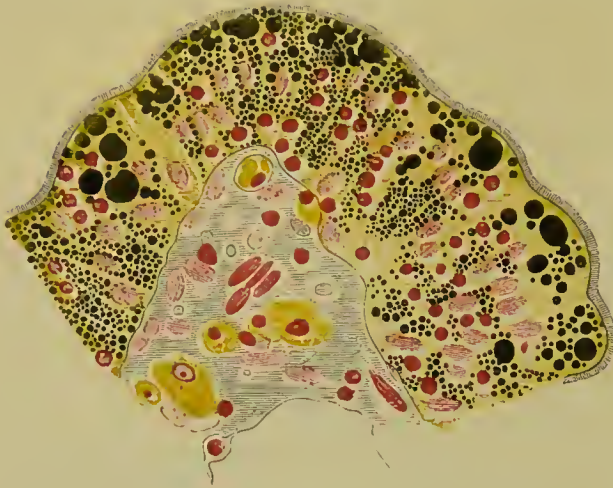


Fig. 260.

Vertical section of the epithelium of a villus, showing the absorption of fat; the fatty particles are blackened by osmic acid.

Krehl, doubt whether fat is absorbed in a particulate form from the intestine, and they regard it as most probable that the fat is absorbed by the epithelium in a soluble form.]

[C. Bernard noticed in rabbits, in whom the chief pancreatic duct opens separate from the bile-duct, and low down in the intestine, that the lacteals first

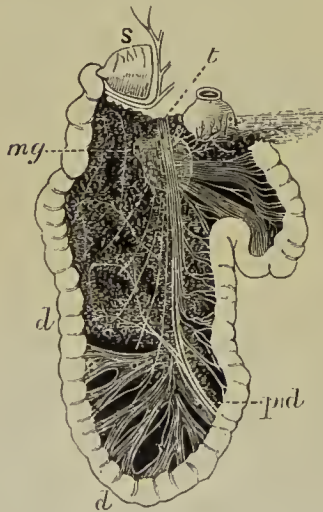


Fig. 261.

Pancreas and duodenum of rabbit during digestion of fat. S, stomach; mg, mesenteric gland; t, lacteals; d, duodenum; pd, entrance of pancreatic duct.

became white below the entrance of the pancreatic duct (fig. 261). This observation led him to attach great importance to the emulsionising properties of the pancreatic juice.]

Fate of the Fats.—The excessively fine fatty particles are used up by the tissues, but all tissues do not do so equally. They are taken up in large amount by the liver, and least of all by muscle. The tissues are said to split up the fats into glycerin and fatty acids, and these are ultimately oxidised to yield heat chiefly.

With regard to the forces concerned in the absorption of fats, v. Wistinghausen stated that when a porous membrane is moistened with bile, the passage of fatty particles through it is thereby facilitated (p. 334), but this fact alone does not explain the copious and rapid absorption of fats. It is possible that the protoplasm of the epithelial cells is actively concerned in the process, and that it takes the particles into its interior. Perhaps a fine protoplasmic process is thrown out by these cells, just as pseudopodia are thrown out and retracted by lower organisms. [This, however, has

3. In the lacteal.—The so-called “molecular basis” of the chyle is first seen and appears to be formed as the suspended fatty granules pass into the lacteal. No such fine fatty emulsion as occurs in the lacteals is found in the small intestine, nor even in the villus itself.

There is no good reason for believing that fat passes directly into the blood-vessels.]

[Some recent observers, *e.g.*

not been corroborated by a sufficient number of observers.] Perhaps the protoplasm of the epithelial cells, in virtue of its contractility, forces the fatty granules

out of the cells into the spaces of the villi, whence they are carried by the lymph-stream (p. 368), and so through the stomata (?), between the endothelial cells into the central lacteal of the villus. According to this view, the absorption of fatty particles, and perhaps also the absorption of true proteids, is in part due to an active vital process, as indicated by the observations of Brücke and v. Thanhofer. This view is supported by the observation of Grünhagen, that the absorption of fatty particles in the frog is most active at the temperature at which the motor phenomena of protoplasm are most lively. That it is due to simple filtration alone is not a satisfactory explanation, for the amount of fatty particles in the chyle is independent of the amount of water in it. If absorption were chiefly due to filtration, we would expect that there would most probably be a direct relation between the amount of water and fat (*Ludwig and Zawitsky*). [The observations of Watney have led him to suppose that the fatty particles do not pass through the cell protoplasm to reach the lacteal, but that they pass through the *cement substance* between the epithelial cells covering a villus. If this view be correct, and it is highly doubtful if it is, the absorbing surface is thereby greatly diminished. Zuarykin and Schäfer suggest that the leucocytes, which have been observed between the columnar cells of the villi of the small intestine, are carriers of at least part of the fat from the lumen of the gut to the lacteal; they also, perhaps, alter it for further use in the economy. [So far these statements relative to the leucocytes have not been universally accepted; indeed, they are denied by the most recent observers.]

[One of the most remarkable experiments in relation to the absorption of fatty matter is that of I. Munk, and confirmed by Walther, viz., that if a dog be fed on **fatty acids** instead of neutral fats, then neutral fats appear in the chyle collected from the thoracic duct. Where does the glycerin come from, and where and how is the synthesis effected? So far there is no satisfactory answer to these questions, but it is suggested that the synthesis takes place in the villi, or even in the lumen of the gut.]

[A most remarkable case of a lymph fistula in man was experimented on by Munk. A lad suffering from elephantiasis had a fistula in the leg, through which during digestion much chyle was discharged. When erucic acid—an acid not found normally in the body—was administered to the lad, the chyle discharged from the fistula did not contain more than traces of free erucic acid, but on the contrary, it contained a large quantity of the corresponding neutral fat erucin. The erucic acid must have somewhere obtained glycerin to combine with, to form the neutral fat. This confirms Munk's experiments on animals, that fatty acids do not reach the blood as such, but that, perhaps, in the very act of absorption in the intestinal mucous membrane, they are by synthesis converted into neutral fats. The case has also been used to prove that sugars when given by the mouth, are all, except an excessively small amount, absorbed by the blood-stream, and do not reach the blood through the lymph- and chyle-stream.]

[**Methods.**—**A. Histological.**—The absorption of fat has usually been studied by feeding an animal on fatty food and examining its villi either in a fresh condition, or more usually after they have been submitted to the action of osmic acid, which blackens fatty matter. In this connection it is important to remember two facts, viz., that turpentine may discharge the black colour of fat acted on by osmic acid, such sections in histological processes being often treated with turpentine; and secondly, an observation of Heidenhain's that osmic acid blackens also granules in some of the leucocytes of the villi which are certainly not fatty, for they are not soluble in ether.]

[**B. Experimental.**—If in a dog a cannula be introduced into the thoracic duct where it joins the subclavian vein, the amount of chyle that flows out in a given time can be estimated. The amount flowing out is not greater during digestion than in a fasting animal. In a fasting animal the fluid is transparent and like lymph, and it becomes white and opaque during digestion from the presence of fatty particles. During the digestion of sugar the chyle does not contain more sugar—0.1–0.2 per cent.—than is present in the lymph or serum of a fasting animal. These and other similar experiments make it clear that the fats alone pass *via* the chyle-stream to reach the blood, all the other products of digestion pass directly into the rootlets of the portal vein.]

The activity of the cells of the intestine with pseudopodial processes may be studied in the intestinal canal of *Distomum hepaticum*. Sommer has figured these pseudopodial processes actively engaged in the absorption of particles from the intestine.

193. INFLUENCE OF THE NERVOUS SYSTEM ON ABSORPTION.—

With regard to the influence of the nervous system upon intestinal absorption, we know very little. After extirpation of the semi-lunar ganglion, as well as after section of the mesenteric nerves (*Moreau*), the intestinal contents become more fluid, and are increased in amount (§ 183). This may be partly due to diminished absorption. *V. Thanhofer* states that he observed the protrusion of threads from the epithelial cells of the small intestine only after the spinal cord, or the dorsal nerves, had been divided for some time.

194. “NUTRIENT ENEMATA.”—In cases where food cannot be taken by the mouth, *e.g.*, in stricture of the œsophagus, continued vomiting, &c., food is given *per rectum*. As the digestive activity of the large intestine is very slight, fluid food ought to be given in a condition ready to be absorbed, and this is best done by introducing it into the rectum through a tube with a funnel attached, and allowing the food to pass in slowly by its own weight. The patient must endeavour to retain the enema as long as possible. When the fluid is slowly and gradually introduced, it may pass above the ileo-cæcal valve.

Solutions of grape-sugar, and perhaps a small amount of soap solution, are useful; and amongst nitrogenous substances the commercial flesh-, bread-, or milk-peptones of *Sanders-Ezn.* and *Adamkiewicz*, in Germany, and *Darby's* fluid meat, and *Carrick's* beef-peptonoids in this country, are to be recommended. The amount of peptone required is 1.11 gm. per kilo. of body-weight (*Catillon*); less useful are butter-milk, egg-albumin with common salt. *Leube* uses a mixture of 150 grms. flesh, with 50 grms. pancreas, 100 grms. water, which he slowly injects into the rectum, where the proteids are peptonised and absorbed. [Peptonised food prepared after the method of *Roberts* is very useful (§ 172).] The method of nutrient enemata only permits imperfect nutrition, and at most only $\frac{1}{4}$ of the proteids necessary for maintaining the metabolism of the body is absorbed (*v. Voit, Bauer*).

195. CHYLE-VESSELS AND LYMPHATICS.—**Lymphatics.**—Within the tissues of the body generally, and even in those tissues which do not contain blood-vessels, *e.g.*, the cornea, or in those which contain few blood-vessels, there exists a system of vessels or channels which contain the juices of the tissues, and within these vessels the fluid always moves in a centripetal direction. These canals arise within the tissues in a variety of ways, and unite in their course to form delicate and afterwards thicker tubes, which ultimately terminate in two large trunks which open at the junction of the jugular and subclavian veins; that on the left side is the **thoracic duct**, and that on the right, the **right lymphatic trunk**.

[Through the thin-walled blood-capillaries there transudes into the spaces of the surrounding tissues part of the blood-plasma. This fluid is the **lymph**. It permeates every tissue of the body, bathing their constituent form-elements, supplying the latter with nutriment, and enabling them to get rid of the waste products resulting from their metabolism. The lymph is collected and returned to the blood in special tubes, the **lymphatics**. Whatever the mode of origin of the lymphatics (p. 376), at first they form thin-walled microscopic lymphatic vessels, which communicate freely with each other in a plexiform manner, and by their confluence they form the lymphatic vessels (.1–1 mm.), which usually run along with the superficial and deep blood-vessels (fig. 262). The larger lymphatics are provided with **valves**, like some veins. The valves open towards the heart, and on the cardiac side of the valve there is a dilatation, so that the lymphatic trunks, especially when injected, often present a beaded or varicose appearance. The walls often are so thin and translucent that one can see the clear lymph which they contain. A moderate-sized **lymphatic trunk** has **three coats** like a vein, only the coats are thinner. The inner coat, or **tunica intima**, consists of a layer of endothelial cells, often with a sinuous outline, resting on a delicate network composed of fine elastic fibres. The middle coat, or **tunica media**, is composed of smooth muscular fibres arranged transversely or obliquely. The **tunica adventitia** consists of connective-tissue, which in some situations contains smooth muscular fibres. The fine lymphatic capillaries have dilatations and constrictions on them, and are composed of a

single layer of endothelium, the edges of which are usually sinuous, a fact best demonstrated by the use of silver nitrate (fig. 263).]

The **lymph** fulfils different functions in different organs. (1) In many tissues, the lymphatics represent the **nutrient channels**, by which the fluid that transudes through the neighbouring vessels is distributed, as in the cornea and in many connective-tissues. (2) In many tissues, as in glands, *e.g.*, the salivary glands and the testis, the lymph-spaces are the chief **reservoirs for fluid**, from which the cells during the act of secretion derive the fluid necessary for that process. (3) The lymphatics have the general function of collecting the fluid which saturates the tissues, and carrying it back again to the blood. The **capillary blood system** may be regarded as an **irrigation system**, which supplies the tissues with nutrient fluids, while the **lymphatic system** may be regarded as a **drainage apparatus**, which conducts away the fluids that have transuded through the capillary walls. Some of the decomposition-products of the tissues, proofs of their retrogressive metabolism, become mixed with the lymph-stream, so that the lymphatics are at the same time **absorbing vessels**. Substances introduced into the parenchyma of the tissues in other ways, *e.g.*, by subcutaneous injection, are partly absorbed by the lymphatics. A study of these conditions shows that the lymphatic system represents an **appendix to the blood-vascular system**, and further that there can be no lymph system when the blood-stream is completely arrested; it acts only as a part of the whole, and with the whole.

Lacteals.—When we speak of the lymphatics proper as against the **chyle-vessels** or **lacteals**, we do so from anatomical reasons, because the important and considerable lymphatic channels coming from the whole of the intestinal tract are, in a certain sense, a fairly independent province of the lymphatic vascular area, and are endowed with a *high absorptive activity*, which from ancient times has attracted the notice of observers. The contents of the chyle-vessels or lacteals are mixed with a large amount of fatty granules, giving the **chyle** a *white* appearance, which distinguishes them at once from the true lymphatics with their clear watery contents. From a physiological point of view, however, the lacteals must be classified with the lymphatics, for, as regards their structure and function, they are true lymphatics, and their contents consist of true lymph mixed with a large amount of absorbed substances, chiefly fatty granules. [The contents of the lacteals

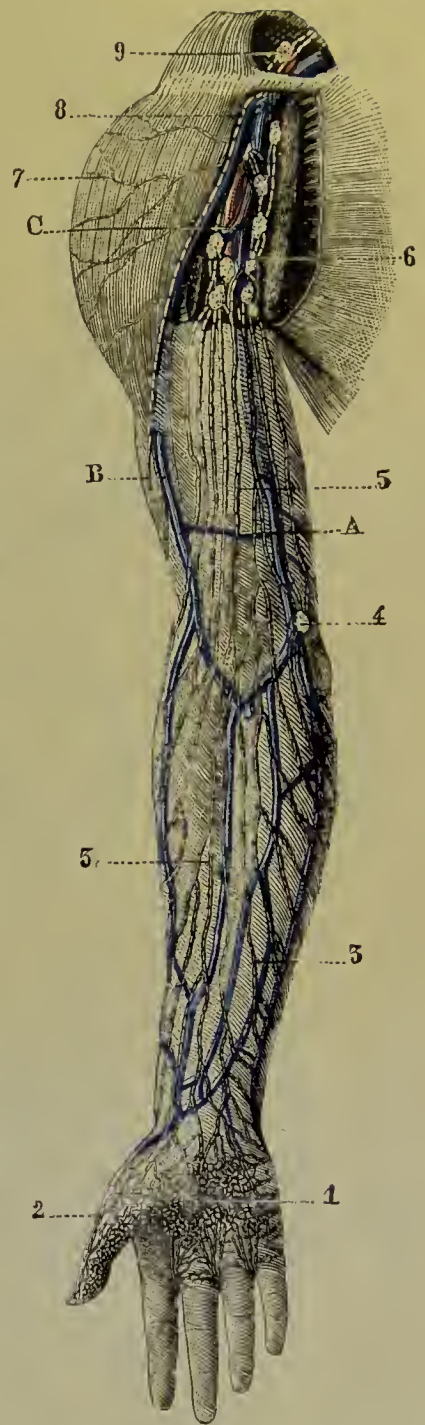


Fig. 262.

Anterior view of the lymphatics of the arm. A, basilic, B, cephalic, and C, axillary veins; 1, lymphatic plexus of the palm; 2, external collateral trunk of the thumb; 3, 3, superficial lymphatics of the forearm, and 5, of the upper arm; 4, supra-trochlear; 6, axillary ganglia; 7, lymphatics of the shoulder; 8, vein accompanying the cephalic vein; 9, ganglia of the neck.

are white only during digestion, at other times, *i.e.*, when an animal has fasted for some time, they are clear like lymph.]

196. ORIGIN OF THE LYMPHATICS—Connective-tissue.—(1) Origin in



Fig. 263.

Lymphatic of the pericardium; epithelium stained with silver, and showing the bulging and constrictions in the vessel.

ment of the lymph is provided for. The cells which lie in the spaces exhibit amœboid movements. Some of these cells remain permanently each in its own

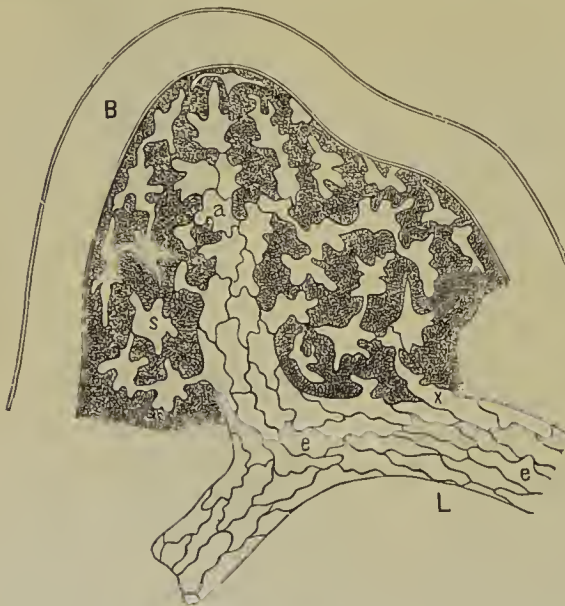


Fig. 264.

Origin of lymphatics from the central tendon of the diaphragm stained with nitrate of silver. *s*, the juice-canals, communicating at *a* with the lymphatics; *a*, origin of the lymphatics by the confluence of several juice-canals.

istic **sinuous margins**, whose characters are easily revealed by the action of silver nitrate (fig. 265, L). This substance blackens the cement-substance which holds

Spaces.—Within the connective-tissues (connective-tissue proper, bone) are numerous stellate, irregular, or branched spaces, which communicate with each other by numerous tubular processes (fig. 264, *s*); in these communicating spaces or **lymph-spaces** lie the cellular elements of these tissues. These spaces, however, are not completely filled by the cells, but an interval exists between the body of the cell and the wall of the space, which is greater or less according to the condition of movement of the protoplasmic cell. These spaces are the so-called "**juice canals**" or "**Saft-canälchen**," and they represent the origin of the lymphatic vessels (*v. Recklinghausen*). As they communicate with neighbouring spaces, the move-

space, within which, however, it may change its form—these are the so-called "**fixed connective-tissue corpuscles**," and bone corpuscles—while others merely wander or pass into these spaces, and are called "**wandering cells**," or "**leucocytes**;" but the latter are merely lymph-corpuscles, or colourless blood-corpuscles which have passed out of the blood-vessels into the origin of the lymphatics (fig. 266). These cells exhibit amœboid movements. These spaces communicate with the small tubular lymphatics—the so-called **lymph-capillaries** (L). The spaces lie close together, where they pass into a lymph-capillary (*a*). The lymph-capillary, which is usually of greater diameter than the blood-capillary, generally lies in the middle of the space within the capillary arch (B). The finest lymphatics are lined by a layer of delicate, nucleated, endothelial cells (*e, e*), with character-

the endothelial cells together. Between the endothelial cells are small holes, or **stomata**, by means of which the lymph-capillaries communicate (at *x*) with the juice-canals.

From the researches of Arnold, Thoma, and others it is assumed that the blood-vessels communicate with the juice-canals, and that fluid passes out of the thin-walled capillaries through their stomata into these spaces (§ 65). This fluid nourishes the tissues, the tissues take up the substances appropriate to each, while the effete materials pass back into the spaces, and from these reach the lymphatics, which ultimately discharge them into the venous blood.

Whether the cells within these spaces are actively concerned in the pouring out of the blood-plasma, or take part in its movement, is matter of conjecture. We can imagine that by contracting their body, after it has been impregnated with fluid, this fluid may be propelled from space to space towards the lymphatics. The leucocytes wander through these spaces until they pass into the lymphatics. Fine particles which are contained in these spaces—*e.g.*, after tattooing the skin, and even fatty particles after inunction—are absorbed by the leucocytes, and carried by them to other parts of the body. [The pigment particles used to tattoo the finger are usually found within the first lymphatic gland at the elbow].

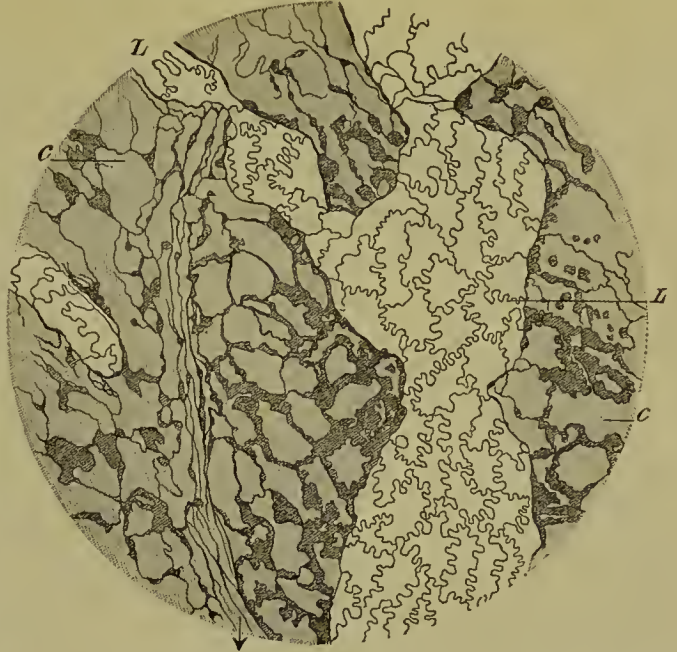


Fig. 265.

Pleural surface of the central tendon of the diaphragm of the rabbit stained with silver nitrate. L, lymphatic with its sinuous endothelium; c, cells of the connective-tissue brought into view by the silver nitrate.

The migration of cellular elements from the blood-vessels into the origin of the lymphatics is to be considered as a normal process. *Granular colouring-matter* passes from the blood into the protoplasmic body of the cells within the lymph-spaces; and only when the granular pigment is in large amount does it appear as a granular injection in the branches of the juice-spaces.

[**Connective-tissue** is widely distributed in the body entering into the construction of most organs, and, as its name denotes, it connects and binds structures together. It assumes many forms, being either of a more or less open texture, when it is called areolar tissue, or its fibres may be so arranged as to form dense membranes, such as fasciæ, or stout cords and bands, like ligaments. It performs certain purely mechanical and certain physiological functions in the economy. It is developed from the cells of the mesoblast, and consists of—

1. Cells or corpuscles.
2. An inter-cellular matrix.

The corpuscles—of which there are several varieties—are in the adult far less numerous than the matrix or inter-cellular matter, which consists of **fibres**, the fibres being of two kinds—the **white fibres** and the **yellow** or **elastic fibres**.

Its mechanical functions depend far more on the fibres than the cells. In the form which occurs under the skin, and surrounds lymphatics and blood-vessels in their course, and is spoken of as **loose connective-tissue** or **areolar tissue**, the fibres are arranged in bundles which cross each other in various directions and leave larger or smaller spaces, or areolæ, between them. These spaces contain lymph, and from them the lymphatics arise, hence the name "areolar." The fixed connective-tissue corpuscles lie on the bundles of white fibres (fig. 266). If a piece of areolar tissue be teased out and examined microscopically, it is seen to consist of bundles of wavy fibres, and these fibres readily split up under the action of reagents, *e.g.*, 10 per cent. common salt or picric acid, into fine

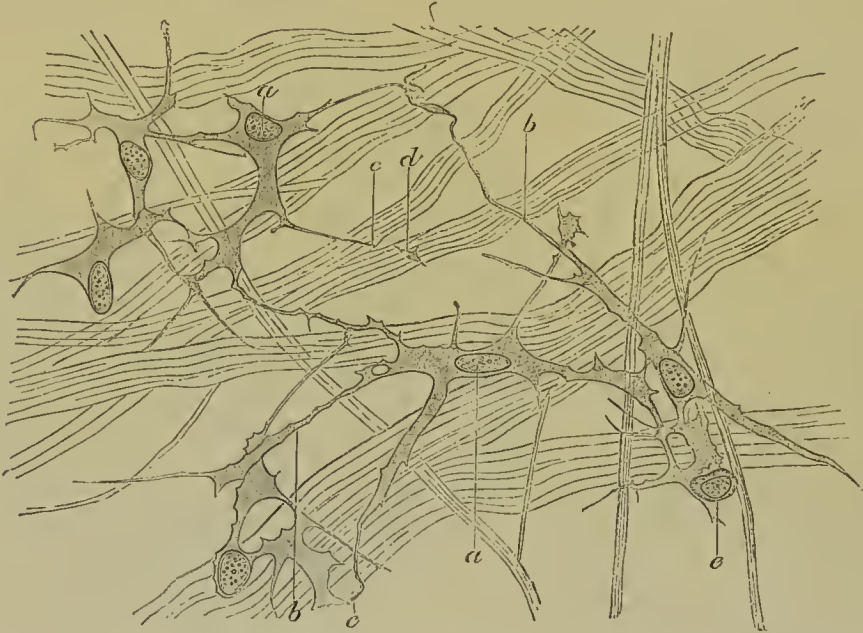


Fig. 266.

Subcutaneous connective-tissue of a sheep. *aa*, fixed connective-tissue corpuscles with processes; *bb*, anastomosing processes; *cc*, broken-off processes; *d*, isolated parts of the cells; *e*, lymph-cell or leucocyte. $\times 800$.

unbranched excessively narrow fibrils or **fibrillæ**, 1μ or less in diameter. The fibrillæ are held together by a globulin-like, or perhaps mucin-like, cement, and according to the number of fibrillæ so is the size of the fibres. The outline of the fibre is always somewhat indistinct, but they refract the light pretty strongly and appear whitish under the microscope, hence their name of **white fibres**. These fibres when boiled yield **gelatin**, and hence they have been called gelatiniferous fibres. The bundles are held together by a cement-substance which is blackened by silver nitrate, and on the fibres lie the **fixed connective-tissue corpuscles** (fig. 267) embedded in the cement. These nucleated cells may be fusiform, but they are more frequently irregular in form and branched. They resemble flattened, winged, or stellate plates. As they are sometimes in relation with more than one fibre, they may present a winged appearance. They are most abundant and most readily seen in young tissue, and are not so readily seen in a preparation from an adult animal, partly because of the number of fibres, and partly because their refractive index is not such as to make them readily visible. If they be stained, however, *e.g.*, with eosin (fig. 266), or if the tissue be acted on by a dilute acid—*e.g.*, acetic acid—the white fibres swell up and become clear and homogeneous, so that the nuclei of the connective-tissue corpuscles come distinctly into view.

The corpuseles become somewhat shrunken and more granular under the action of the acid. These are called "fixed" connective-tissue corpuseles because they do not change their place, nor do they in the adult exhibit amœboid movement. In the spaces of areolar tissue there are always found some cells much smaller than the foregoing, spherical in form, and presenting all the characters of **leucocytes**, which indeed they are (fig. 266, *e*). They exhibit amœboid movements and have wandered out of the blood-vessels or lymphatics into the areolar spaces. A third form of corpusele is frequently found, more especially along the course of the smaller blood-vessels in certain situations. The last variety of cells always contains numerous large granules. These cells were called "**plasma cells**" by Waldeyer.]

[In the connective-tissue of the mesentery of the newt, and in the peri-œsophageal membrane around the œsophagus of the frog, and in the connective-tissue membranes of vertebrates generally, Ranvier has described some enormously large connective-tissue corpuseles—nearly 1 mm. in size—which stain deeply with methyl-violet. He has called them "**clasmatocytes**" (κλάσμα, ατος, fragment, κύτος, cell), because they tend to break up into small particles or granules. What their relation is to other forms of connective-tissue corpuseles has not been determined.]

[**Clasmatocytes** occur in the thin connective-tissue membranes of vertebrata, and are most readily found in the peri-œsophageal membrane of the frog. They are first fixed with osmic acid and then stained with methyl-violet, 5 B. In the triton they are about 1 mm. in length, and are therefore colossal cells. When stained they are coloured violet with a tinge of red, the nucleus being slightly blue. They have numerous processes, simple or branched, but the processes do not form a reticulum. The body and processes have a granular appearance and are irregular in their shape. Parts of them tend to separate in fragments, hence the name of the cells. This is the peculiarity of these cells, that their processes tend to break up and form islands of granules under certain conditions, and this process Ranvier calls **elasmaeytosis**. They do not exhibit amœboid movements, although they are developed by the evolution of leucocytes, which have passed out of the vessels into the connective-tissue. Ranvier has traced the stages from the simple leucocytes up to these complex and marvellous cells. The elasmatoeyte is at least one hundred times larger than the leucocyte. Certain leucocytes, after reaching the meshes of the connective-tissue, appear to grow, enlarge, and undergo a particular evolution which makes them elasmatoeytes, which give off part of their substance in fragments, which are probably used in the economy (*Ranvier*).]

[It is difficult to say what is the relation—if any—of these cells to the plasma-cells of Waldeyer, *i.e.*, certain granular cells situated along the course of the blood-vessels, the interstitial cells of the testes, and the cells of the supra-renal capsules (p. 176). Ehrlich, by staining the plasma-cells with aniline dyes, showed that they were not all alike. Only some of them were coloured by the basic aniline dyes; these are the anilinophile cells or "**Mastzellen**" of Ehrlich. They are derived from the fixed connective-tissue corpuseles.]

[There are also **yellow** or **elastic fibres** present in areolar tissue. They can be seen in a fresh preparation of the tissue, but are best seen after the action of acetic acid, which makes the white fibres transparent, but does not affect the yellow fibres. The yellow fibres are not so numerous as the white; they have a sharper outline, and faint yellow tinge; they branch and anastomose, and when broken tend to curl up at their ends. By their anastomoses they form networks which render the tissues in which they occur more or less elastic. They vary in size, but they cannot be split up further into fibres. In some situations the elastic fibres become

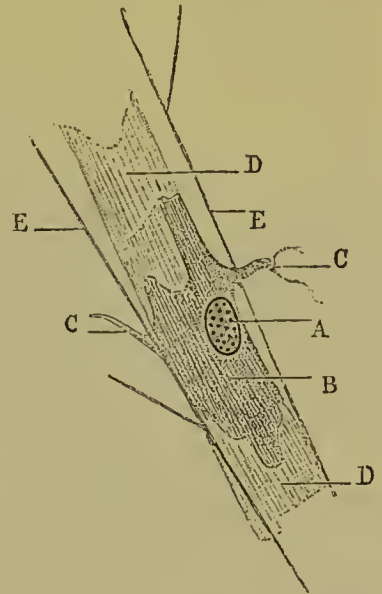


Fig. 267.

Showing relation of a connective-tissue corpusele to a fibre, lying on and clasping the latter. A, nucleus of the fixed cell; B, protoplasm body; C, processes; D, white fibre on which the cell rests; E, elastic fibre. $\times 1000$.

greatly increased both in number and size, as in the ligamentum nuchæ, which consists almost entirely of elastic fibres—some of them as broad as a red blood-corpuscle (fig. 269). There is every gradation between the fine networks of elastic fibres that occur in the meso-colon and skin (fig. 268) to the thick fibres of the ligamentum nuchæ, up to fenestrated sheets of elastic tissue occurring in the



Fig. 268.

Network of yellow or fine elastic fibres from the omentum. Some corpuscles are also visible. $\times 350$.

which traverse the lymph-space and become attached to the wall of the included blood-vessel. Fig. 270, B, represents a transverse section of a small blood-vessel, B, from the brain; *p* is the divided perivascular space. This space is called

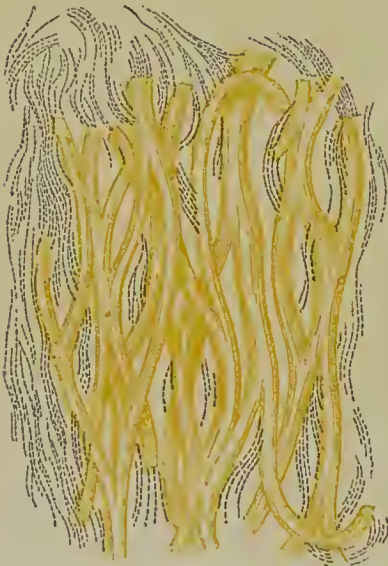


Fig. 269.

Thick elastic fibres of the human ligamentum nuchæ. $\times 459$.

the **perivascular space** of His, but in addition to it the blood-vessels of the brain have a lymph-space within the adventitia of the blood-vessels (*Virchow-Robin's space*). It is partly lined by well-defined endothelium. Where the blood-vessels begin to increase considerably in diameter, they pass through the wall of the lymphatics, and the two vessels afterwards take separate courses. In all cases, where there is a perivascular space, the passage of lymph- and blood-corpuscles into the lymphatics is greatly facilitated. In the tortoise the large blood-vessels are often surrounded with perivascular lymphatics. Fig. 270, A, gives a representation of the aorta of the tortoise surrounded by a perivascular space which is visible to the unaided eye. In mammals the perivascular spaces are microscopic.

(4) **Origin in the form of interstitial slits within organs.**—Within the testis the lymphatics begin simply in the form of numerous slits, which occur between the coils and twists of the seminal tubules. They take the form of elongated spaces bounded by the curved cylindrical surfaces

aorta, and the complete sheet of elastic membrane, forming the chief part of the elastic lamina of the arteries. The elastic fibres consist of **elastin** (§ 250).]

(2) **Origin within villi**—*i.e.*, of the chyle vessel or lacteal—has been described (§ 190).

(3) **Origin in perivascular spaces** (fig. 270). — The smallest blood-vessels of bone, the central nervous system, retina, and the liver, are completely surrounded by wide lymphatic tubes, so that the blood-vessels are completely bathed by a lymph-stream. In the brain these lymphatics are partly composed of delicate connective-tissue fibres,

of the tubules. The surfaces, however, are covered with endothelium. The lymphatics of the testis get independent walls after they leave the parenchyma of the organ. In many other glands the gland-substance is similarly surrounded by a lymph-space. The blood-vessels pour the lymph into these spaces, and from them the secreting cells obtain the materials necessary for the formation of their secretion.

(5) **Origin by means of free stomata** on the walls of the larger serous cavities, which (fig. 271, *a*) communicate freely with the lymphatics. The investigation of the serous surfaces is most easily accomplished on the septum of the great abdominal lymph-sac of the frog. Silver nitrate reveals the presence of relatively large free openings or **stomata** lying between the endothelium. Each stoma is bounded by several **germinating cells**, which have a granular appearance, and undergo a change of shape, so that the size of the stoma depends upon the degree of contraction of these cells; thus the stoma may be open (*a*), half-open (*b*), or completely closed (*c*). These stomata are the origin of the lymphatics. The serous cavities belong therefore to the lymphatic system, and fluids placed in the serous

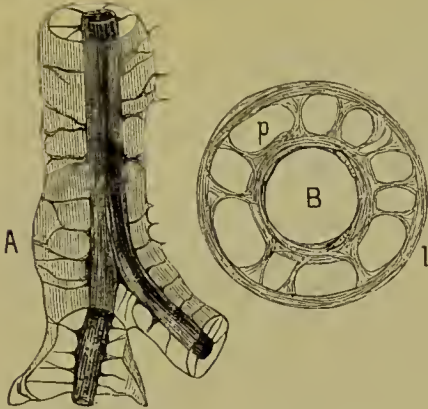


Fig. 270.

Perivascular lymphatics. A, aorta of tortoise; B, artery from the brain.

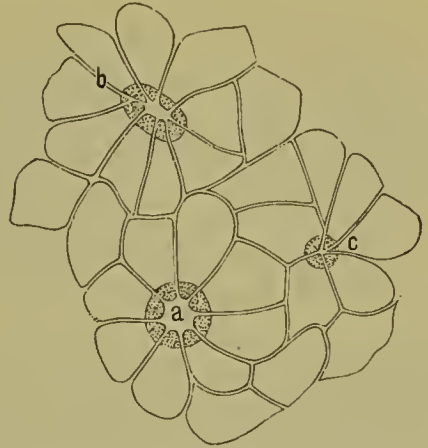


Fig. 271.

Stomata in the great lymph-sac (frog). *a*, open; *b*, half-closed; *c*, closed.

cavities readily pass into the lymphatics. The cavities of the peritoneum, pleura, pericardium, tunica vaginalis testis, arachnoid space (?), aqueous chambers of the eye, and the labyrinth of the ear, are true lymph-cavities, and the fluid they contain is to be regarded as lymph. [Hoffmann has found that a nerve-fibre surrounds the stomata in the frog and sends branches between the germinal epithelium.]

(6) **Free open pores** have been observed on some **mucous membranes**, which are regarded as the origin of lymphatics, *e.g.*, in the bronchi, nasal mucous membrane, trachea, and larynx.

Structure of Lymphatics.—The larger lymphatics resemble in structure the veins of corresponding size. The **valves** are particularly numerous in the lymphatics, so that a distended lymphatic resembles a chain of pearls (p. 371). [Lymphatics have dilations here and there in their course (fig. 265).]

197. THE LYMPH-GLANDS.—The **lymphatic glands** belong to the lymph apparatus. They are incorrectly termed glands, as they are merely much-branched lacunar labyrinthine spaces composed of adnoid tissue, and intercalated in the course of the lymphatic vessels. There are **simple** and **compound** lymph-glands.

(1) The **simple lymph-glands**, or, more correctly, **lymph-follicles**, are small rounded bodies, about the size of a pin-head. They consist of a mass of adnoid tissue (fig. 272, A), *i.e.*, of a very delicate network of fine reticular fibres with nuclei at their points of intersection, and in the spaces of the meshwork lie the lymph and the lymph-corpuscles. Near the surface the tissue is somewhat denser, where it forms a capsule, which is not however a true capsule, as it is permeated with numerous small sponge-like spaces. Small lymphatics come directly into contact with these lymph-follicles, and often cover their surface in the form of a

close network. The surface of the lymph-follicles is not unfrequently placed in the wall of a lymph-vessel, so that it is directly bathed by the lymph-stream. Although no direct canal-like opening leads from the follicle into the lymphatic stream in relation with it, a communication must exist, and this is obtained by the numerous spaces in the follicle itself, so that a lymph-follicle is a true lymphatic apparatus whose juices and lymph-corpuscles can pass into the nearest lymphatic. The follicles are surrounded by a network of blood-vessels which sends loops of capillaries into their interior (fig. 272, B). [In the centre of each is a germ-centre where mitosis goes on rapidly.] We may assume that lymph-corpuscles pass from these capillaries into the follicle.

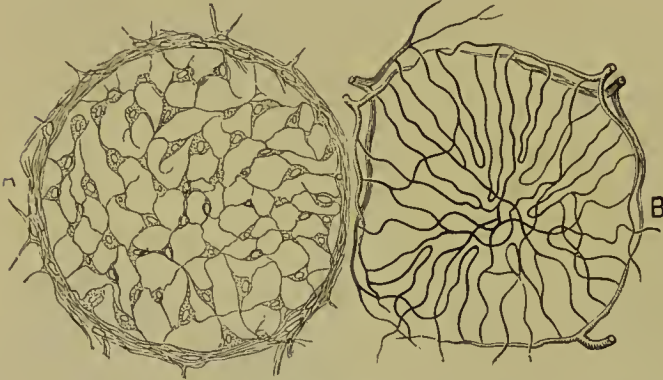


Fig. 272.

Two lymph-follicles. A, a small follicle highly magnified, showing the adenoid reticulum; B, a follicle less highly magnified, showing injected blood-vessels.

[The follicles arise by aggregation of round cells or leucocytes in the mucosa or sub-mucosa, where they rapidly reproduce themselves by mitosis. The gradually enlarging mass compresses the surrounding tissue which forms a kind of tunica propria for each follicle (p. 239). In the intestine the cupola is covered by columnar epithelium with a few goblet-cells.]

the back of the tongue, the solitary glands of the intestine, and the adenoid tissue in the bronchial tract, the tonsils, and Peyer's patches, it is important to

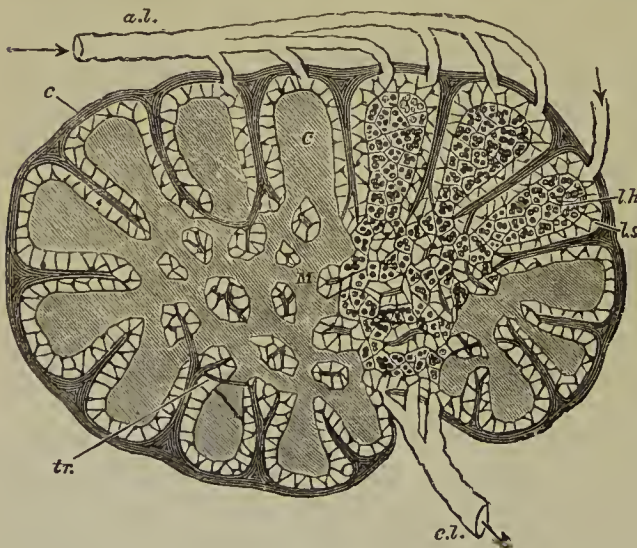


Fig. 273.

Diagrammatic section of a lymphatic gland. *a.l.*, afferent, *e.l.*, efferent, lymphatics; *C*, cortical substance; *M*, reticular cords of medulla; *l.s.*, lymph-sinns; *c*, capsule, with trabeculae, *tr*.

In connection with these follicles, including those of the intestine, and the adenoid tissue in the bronchial tract, the tonsils, and Peyer's patches, it is important to remember that enormous numbers of leucocytes pass out continually between the epithelial cells covering these follicles. In this process many epithelial cells are destroyed. Thus there is a kind of physiological solution of continuity of the surface, through which, under certain conditions, micro-organisms or other poisonous bodies may enter the organism. The extruded leucocytes undergo disintegration subsequently.

(2) The **compound lymph-glands—the lymphatic glands**—represent a collection of lymph-follicles, whose form is somewhat altered. [They are small oval or kidney-shaped bodies varying much in size, and intercalated in the course

of lymphatics. Usually at one side there is a *hilum* from which the efferent lymphatic issues.] Every lymph-gland is covered externally with a connective-tissue capsule (fig. 273, *c*), which contains numerous non-striped muscular fibres. From

its inner surface numerous **septa** and **trabeculae** (*tr.*) pass into the interior, so that the gland-substance is divided into a large number of **compartments**. These compartments in the *cortical* portion of the gland have a somewhat rounded form, and are nearly filled with aggregations of lymph-corpuscles, sometimes called **secondary nodules**—which constitute the alveoli, while in the medullary portion they have



Fig. 274.

Network of adenoid tissue. The leucocytes have been pencilled out of the meshes (*Stirling*). $\times 350$.

a more elongated and irregular form. [In many of the nodules there is a lighter centre—**germ-centre**—where mitosis or division of the leucocytes goes on rapidly (fig. 275). On making a section of a lymph-gland we can readily distinguish the **cortical** from the **medullary** portion of the gland.] All the compartments are of equal dignity, and they all communicate with each other by means of openings, so that the septa bound a rich network of spaces within the gland, which communicate on all sides with each other.

These spaces are traversed by the follicular threads (fig. 276, *f, f*). These represent the contents of the spaces, but are smaller than the spaces in which they lie, and do not come into contact anywhere with the walls of the spaces. If we imagine the spaces to be injected with a mass, which ultimately shrinks to one-half of its original volume, we obtain a conception of the relation of these follicular threads to the spaces of the gland.

[The **blood-vessels** of the gland (*b*) lie within these follicular threads. They are surrounded by a tolerably thick crust of adenoid tissue, with very fine meshes (*x, x*) filled with lymph-corpuscles, and with its surface (*o, o*) covered by the cells of the adenoid reticulum, in such a way as to leave free communication through the narrow meshes. The blood-vessels may enter at the hilum or at points on the surface of the gland.

The large branches run in the trabeculae and septa, and from these finer branches traverse the lymph-paths and split up into a capillary plexus in the masses or strands of adenoid tissue. The vein passes out by the hilum. **Nerves**, medullated and non-medullated, enter the gland, but their terminations are unknown. Perhaps they go to the blood-vessels and the smooth muscular fibres of the septa.]

[The fine network of **adenoid tissue** which traverses the lymph-paths, and in

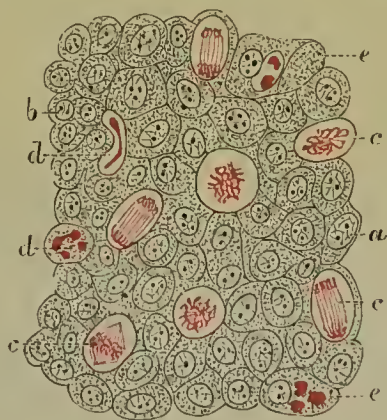


Fig. 275.

Section of a lymph-knot, or germ centre of a mesenteric lymph-gland. *a*, large, *b*, small leucocytes; *c*, mitosis; *d*, direct division of nucleus; *e*, cells which, besides a nucleus, contain large easily-stained bodies and some yellow granules. $\times 400$.

which the leucocytes lie, consists of fine bundles of fibrous tissue with cells—endothelial cells—at the nodes. This system is continuous with the fibrous tissue of the capsule and septa (fig. 274).]

[The **cellular elements**, **lymph-cells**, or **leucocytes** are not all of one kind, as can be shown by differential staining, such as Ehrlich-Biondi's fluid, which is a mixture of orange-G., methyl-green, and acid fuchsine. The most abundant leucocytes are (1) cells with a very small amount of colourless protoplasm surrounding a faint violet-stained nucleus. (2) A second form has a large nucleus surrounded with bright rose-coloured protoplasm. (3) There are "granular" cells most abundant in the mesenteric glands. (4) A fourth form shows cells undergoing degeneration.



Fig. 276.

Part of a lymphatic gland. A, vas afferens; B, B, lymph-paths; a, a, trabeculae seen on edge; f, f, follicular strand from the medulla; x, x, its adenoid reticulum; b, its blood-vessels; o, o, narrow-meshed part limiting the follicular strands from the lymph-path.

(5) Phagocytes are also present, but they are usually found in the lymph-paths and medullary cords (*Hoyer*).]

Lymph-glands not only form leucocytes, but in them also cells break down, and the products of their disintegration are taken up by leucocytes and further changed by them.

Between the surface of the follicular threads and the inner wall of all the spaces of the gland, lies the **lymph-channel** or **lymph-path** (B, B), which is traversed by a reticulum of adenoid tissue, containing relatively few lymph-corpuseles. It is very probable that these lymph-paths are lined by endothelium.

The **vasa afferentia** (fig. 273, *a.l.*), of which there are usually several, expand upon the surface of the gland, perforate the outer capsule, and pour their contents into the lymph-paths of the gland (C). The **vasa efferentia**, which are less numerous than the afferentia, and come out at the hilum, form large, wide, almost

cavernous dilatations, and they anastomose near the gland (*e.l.*). Through them the lymph passes out at the opposite surface of the gland. The lymph percolates through the gland, and passes along the lymph-paths, which represent a kind of rete mirabile interposed between the afferent and efferent lymph-vessels.

During its passage through this complicated branched system of spaces, the movement of the lymph through the gland is retarded, and, owing to the numerous resistances which occur in its path, it has very little propulsive energy. The lymph-corpuscles which lie in the meshes of the adenoid reticulum are washed out of the gland by the lymph-stream. The lymph-corpuscles lying within the follicular threads pass through the narrow meshes (*o*) into the lymph-paths. The formation of lymph-corpuscles either occurs locally, from division of the pre-existing cells, or new leucocytes wander out into the follicular threads. The movement of the lymph through the gland is favoured by the muscular action of the capsule. When the capsule contracts energetically, it must compress the gland like a sponge, and the direction in which the fluid moves is regulated by the position and arrangement of the valves.

[**Formation of leucocytes in lymph-glands.**—This takes place chiefly in the cortical alveoli. In the centre of each is a **germ-centre**, in the form of a spherical group of leucocytes, which stain more deeply with staining reagents than the surrounding leucocytes. These cells divide by **mitosis**, and the chromatin filaments can be stained with saffranin or other chromatin dye (fig. 275). Mitosis takes place to a much less extent in the medullary cords and the cells of the lymph-stream itself.]

Chemistry of lymph-glands.—In addition to the constituents of lymph and leucocytes (§ 24), the following chemical substances have been found in lymphatic glands—leucin and xanthin.

198. PROPERTIES OF LYMPH AND CHYLE.—Lymph is an albuminous, colourless, clear alkaline fluid, containing **lymph-corpuscles**, which are identical with the colourless blood-corpuscles (§ 9). [Its specific gravity is 1012-1022.] In some places, *e.g.*, in the thoracic duct, a few coloured blood-corpuscles have been found. The lymph-corpuscles are supplied to the lymph and chyle from the lymphatic glands and the adenoid tissue. As to their source see § 200, 2. They also pass out of the blood-vessels and wander into the lymphatics. As red blood-corpuscles have also been seen to pass out of the blood-vessels, this explains the occasional presence of these corpuscles in some lymphatics; but when the pressure within the veins is high, near the **central** orifice of the thoracic duct, red blood-corpuscles may pass into the thoracic duct. But we are not entitled to conclude from their pressure that lymph-cells form red blood-corpuscles. In addition, the **chyle** contains numerous **fatty granules**, each surrounded with an albuminous envelope. [Thus the chyle, in addition to the constituents of the lymph, contains, especially during digestion, a very large amount of fat, in the form of the finely-emulsified fat of the food, which gives it its characteristic *white* or milky appearance. During hunger, the fluid in the lacteals resembles ordinary lymph. The fine fat-granules constitute the so-called “**molecular basis**” of the chyle.]

Composition of Lymph.—The lymph consists of **lymph-plasma** with **lymph-corpuscles** suspended in it. The corpuscles or leucocytes are described in § 24. The **lymph-plasma** contains the three so-called fibrin-factors, derived very probably from the breaking up of lymph-corpuscles (§ 29). When lymph is withdrawn from the body, these substances cause it to **coagulate**. Coagulation occurs slowly, owing to the formation of a soft, jelly-like, small “**lymph-clot**,” which contains most of the lymph-corpuscles. The exuded fluid or **lymph-serum** contains *alkali-albuminate* (precipitated by acids), *serum-albumin* (coagulated by heat), and *paraglobulin*—the latter two occurring in less amount but in the same proportion as in the blood-serum; 37 per cent. of the coagulable proteids is paraglobulin.

[After rapid injection of peptone into the blood the lymph does not clot (*Fano*). Peptone injection profoundly alters the endothelial cells of the blood-capillaries.]

[The same organic constituents occur in lymph as in blood-plasma, although in different proportions, but CO₂ and urea are more abundant in lymph than blood. The inorganic constituents are approximately the same in amount and in the same proportions in the two fluids :—

Human Blood-plasma.		Human Lymph.
Water, ...	902.90	986.34
Solids, ...	97.10	13.66
Fibrin, ...	4.05	1.07
Other proteids, ...	78.84	2.30
Extractives, ...	5.66	1.51
Inorganic salts, ...	78.55	8.78.]

(1) **Chyle** is the name given to the fluid which occurs within the lacteals of the intestinal tract during the digestion of fatty food. It can only be obtained in very small amount before it is mixed with lymph, and hence the difficulty of investigating it. A few **lymph-corpuscles** occur even in the origin of lacteals within the villi, but their number increases in the vessels beyond the intestine, more especially after the chyle has passed through the mesenteric glands. The amount of **solids**, which undergoes a great increase during digestion, on the contrary, diminishes when chyle mixes with lymph. After a diet rich in fatty matters the chyle contains innumerable **fatty granules** (2–4 μ in size). [This is the so-called “**molecular basis**” of the chyle.] The amount of *fibrin factors* increases with the increase of lymph-corpuscles as they are formed from the breaking up of the lymph-corpuscles; a *diastatic ferment* absorbed from the intestine; occasionally *sugar*; after much starchy food *lactates*; peptone in the leucocytes (§ 192, I., 3), and traces of urea and leucin. [The chyle contains a greater percentage of solids, as compared with lymph, while the fats are specially abundant in chyle.]

The **Chyle** of a person who was executed contained 90.5 per cent. of water.

Solids, ... 9.5	Fibrin, ...	trace
	Albumin, ...	7.1
	Fats, ...	0.9
	Extractives, ...	1.0
	Salts, ...	0.5

Schmidt found the following **inorganic** substances in 1000 parts of chyle of a horse :—

Sodic chloride, ... 5.84	Sulphuric acid, ... 0.05	Magnesium phosphate, ... 0.05
Soda, ... 1.17	Phosphoric acid, ... 0.05	Iron, ... trace.
Potash, ... 0.13	Calcic phosphate, ... 0.20	

[The following table shows the composition of **chyle** in some animals :—

100 Parts Chyle contains	Man.	Dog.	Horse.
Water, ...	90.5	91.2	92.8
Solids, ...	9.5	8.8	7.2
Fibrin, ...	0.1	0.1	0.1
Proteids, ...	7.0	2.7	4.0
Fat, &c., ...	1.0	4.9	1.5
Extractives, ...	1.4	0.3	0.8
Salts, ...		0.8	0.8
			(Munk).]

[**Extravasations of Chyle and Chylous Ascites.**—After ligature of the thoracic duct in dogs, the receptaculum chyli bursts and the chyle is discharged into the peritoneal cavity. Sometimes there is rupture of the lacteal paths in man, when the chyle passes into the peritoneum, causing chylous dropsy.]

(2) The **lymph** obtained from the beginning of the lymphatic system also con-

tains very few lymph-corpuscles ; it is clear, transparent, and colourless, and closely resembles the fluids of serous cavities. That the lymph coming from different tissues varies somewhat is highly probable, but this has not been proved. After lymph has passed through lymphatic glands, it contains more corpuscles, and also more solids, especially albumin and fat. Ritter counted 8200 lymph-corpuscles in 1 cubic centimetre of the lymph of a dog.

Lymph obtained from a lymphatic fistula in the leg of a man has an alkaline reaction and a saline taste, and the following composition :—

Lymph (Hensen & Dähnhardt).	Cerebro-spinal Fluid (Hoppe-Seyler).	Pericardial Fluid (v. Gorup-Besanez).
Water, ... 98·63	98·74	95·51
Solids, ... 1·37	1·25	4·48
Fibrin, ... 0·11	...	0·08
Albumin, ... 0·14	0·16	2·46
Alkali-albuminate, . . 0·09	...	...
Extractives, { 0·15	...	1·26
Urea, Leucin, { 0·15	The cerebro-spinal fluid and abdominal lymph contain a kind of sugar (?) (without the property of rotating polarised light—Hoppe-Seyler).	
Salts, ... 0·88		
70 vol. % of absorbed CO ₂ , 50 % could be pumped out, and 20 % liberated by the addition of an acid.		

[The following table from Munk shows the composition of lymph in man and some animals—

100 parts of Lymph contain	Man.	Horse.	Ox.
Water, ...	95·0	95·8	96·4
Solids, ...	5·0	4·2	3·6
Fibrin, ...	0·1	0·1	0·1
Proteids, ...	4·1	2·9	2·8
Fats, &c., ...	traces	traces	traces
Extractives, ...	0·3	0·1	0·1
Salts, ...	0·5	1·1	0·6]

100 parts of the ash of lymph contained the following substances :—

Sodium chloride, ... 74·48	Lime, ... 0·98	Sulphuric acid, ... 1·28
Soda, ... 10·36	Magnesia, ... 0·27	Carbonic acid, ... 8·21
Potash, ... 3·26	Phosphoric acid, ... 1·09	Iron oxide, ... 0·06

Just as in blood, **potash** and **phosphoric acid** are most abundant in the corpuscles ; while **soda** (chiefly sodium chloride) is most abundant in the **lymph-serum**. The potash and phosphoric acid compounds are most abundant in cerebro-spinal fluid, according to C. Schmidt. The amount of **water** in the lymph rises and falls with that of the blood.

Gases of Lymph.—Dog's lymph contains much CO₂—more than 40 vols. per cent., of which 17 per cent. can be pumped out, and 23 per cent. expelled by acids, while there are only traces of O and 1·2 vols. per cent. N (*Ludwig, Hammarsten*). See also p. 224.

[The **cerebro-spinal fluid** contains a substance which reduces an alkaline solution of cupric-hydrate. It is not sugar but pyrocatechin. The potassic are in excess of the soda salts, while the fluid of meningococles and chronic hydrocephalus contains proto-albumose, some serum-globulin, no serum-albumin, but the last is present in acute hydrocephalus fluid. No albumose is found in pericardial or pleuritic fluids (*Halliburton*). This fluid is not a simple exudation from the blood. It presents rather the characters of a secretion.]

[**Serosity or Lymph of Serous Cavities.**—Ranvier has made the remarkable discovery that the fluid in normal serous cavities, *e.g.*, the peritoneum, is usually not clear like water, but somewhat turbid or even opalescent. This fluid always contains red blood-corpuscles and several varieties of spherical colourless corpuscles

varying in structure and reactions according to the animal examined. In the fluid from the rabbit's peritoneal cavity, nearly all the colourless cells have the same structure, although their diameter varies from 6 to 20 μ . The largest variety often contains many vacuoles. There are no cells so large either in the lymph or blood. Most of the cells exhibit amœboid movements. If they are lymphatic cells, they have become greatly altered after leaving the vessels and passing into the peritoneal cavity. In the rat also there are colourless cells, some of which are amœboid and others not. The last variety—non-amœboid—is granular and very large, 20–25 μ in diameter, and are readily coloured by fuchsin or methyl-violet. No corresponding cells exist in the rat or rabbit. In the pleuro-peritoneal cavity of reptiles similar large granular cells are found, comparable to those of the rat, but no large granular cells occur in the frog. Ranvier is of opinion that there is a close relationship between true clasmatoocytes (p. 375) and the non-amœboid cells of the serosity of the pleuro-peritoneal cavity.] ;

199. QUANTITY OF LYMPH AND CHYLE.—When it is stated that the total amount of the lymph and chyle passing through the large vessels in twenty-four hours is equal to the amount of the blood, it must be remembered that this is merely a conjecture. Of this amount one-half may be lymph and the other half chyle. The formation of lymph in the tissues takes place continually, and without interruption. Nearly 6 kilos. of lymph were collected in twenty-four hours from a lymphatic fistula in the arm of a woman, by Gubler and Quevenne; 70 to 100 grms. were collected in 1½ to 2 hours from the large lymph-trunk in the neck of a young horse. The following **conditions affect the amount of chyle and lymph**:—

(1) The amount of chyle undergoes very considerable **increase during digestion**, more especially after a full meal, so that the lacteals of the mesentery and intestine are distended with white or milky chyle. During hunger the lymph-vessels are collapsed, so that it is difficult to see the large trunks.

(2) The amount of lymph **increases** especially with the **activity of the organ** from which it proceeds. Active or passive **muscular movements** greatly increase its amount. Lesser obtained in this way 300 cubic centimetres of lymph from a fasting dog, whereby its blood became so inspissated as to cause death.

(3) All conditions which increase the **pressure** upon the juices of the tissues **increase** the amount of lymph, and *vice versâ*. These conditions are:—

(a) An **increase of the blood-pressure**, not only in the whole vascular system, but also in the vessels of the corresponding organ, augments the amount of lymph, and *vice versâ* (*Ludwig, Tomsa*). This, however, is doubtful, as has been shown by Pasehutin and Emminghaus. [In order to increase the amount of lymph depending upon pressure within the vessels, what must happen is increased pressure within the capillaries and veins.]

(b) **Ligature or obstruction of the efferent veins** greatly increases the amount of lymph which flows from the corresponding parts (*Bidder, Emminghaus*). It may be doubled in amount. Tight bandages cause a swelling of the parts on the peripheral side of the bandage, owing to a copious effusion of lymph into the tissue (congestive œdema).

(c) An increased **supply of arterial blood** acts in the same way, but to a less degree. Paralysis of the vaso-motor nerves, or stimulation of vaso-dilator fibres, by increasing the supply of blood increases the amount of lymph; while diminution of the blood-supply, owing to stimulation of vaso-motor fibres or other causes, diminishes the amount. Even after ligature of both carotids, as the head is still supplied with blood by the vertebrals, the lymph-stream in the large cervical lymphatic does not cease.

(4) When the **total amount of the blood** is increased, by the injection of blood or serum into the arteries, much fluid passes into the tissues and increases the formation of lymph.

(5) The formation of lymph still goes on for a short time after death, and after complete cessation of the action of the heart, but only to a slight extent. If fresh blood be caused to circulate in the body of an animal, while it is still warm, more lymph flows from the lymphatics. It appears as if the tissues obtained plasma from the blood for a time after the stoppage of the circulation. This perhaps explains the circumstance that some tissues, *e.g.*, connective-tissues, contain more fluid after death than during life, while the blood-vessels have given out a considerable amount of their plasma after death.

(6) The amount of lymph is increased under the influence of *curare*, and so is the amount of solids in the lymph (*Lesser*). A large amount of lymph collects in the lymph-sacs [especially the sub-lingual] of frogs poisoned with *curare*, which is partly explained by the fact that the lymph-hearts are paralysed by *curare*.

(7) The amount of lymph is also increased in **inflamed parts**.

[(8) Injection of **peptone** into the blood causes a large increase in the rate of flow of lymph. In the thoracic duct it may be increased tenfold, notwithstanding the fall of blood-pressure due to the peptone injected. The amount of solids also increase (*Heidenhain*).]

200. ORIGIN OF LYMPH.—(1) **Source of the Lymph-Plasma.**—The lymph-plasma may be partly regarded as fluid which has been pressed through the walls of the blood-vessels by the blood-pressure, *i.e.*, by **filtration** into the tissues. The *salts* which pass most readily through membranes go through nearly in the same proportion as they exist in blood-plasma—the *fibrin-factors* to about two-thirds, and *albumin* to about one-half of that in the blood (p. 43). As in the case of other filtration-processes, the amount of lymph must increase with increasing pressure.

Ludwig and Tomsa found that when they passed blood-serum under varying pressures through the blood-vessels of an excised testis, the amount of transuded fluid which flowed from the lymphatics varied with the pressure. This “**artificial-lymph**” had a composition similar to that of the natural lymph. Even the amount of albumin increased with increasing pressure. The lymph-plasma is mixed in the different tissues with the decomposition products, the results of the metabolism of the tissues.

[There are reasons for thinking that the formation of lymph is not entirely, or chiefly due to filtration, *i.e.*, it is not merely a transudation from the blood-vessels. By some it is regarded as a **secretory product** of the cells of the capillary wall (*Heidenhain*).]

[When sugar, egg-albumin, peptone, urea, or NaCl are injected into the blood they pass in a concentrated form into the increased lymph-stream. If peptone be injected the blood-pressure falls enormously, still these bodies pass into the lymph, so that their passage cannot be due entirely to blood-pressure. The increase of the lymph under (8) led Heidenhain to regard the formation of lymph not as a transudation, but as a true secretion from the blood-vessels. With the increase of the lymph-stream, the secretion of urine also increases. One may regard the lymph-system as a reservoir which temporarily takes up substances from the blood until they can be excreted by the urine (*Heidenhain*). Peptone when injected slowly into the blood is excreted in the urine, but if the renal vessels are tied it passes from the blood into the lymph. If it be rapidly injected it is chiefly thrown out into the lymph, and after a time it passes from the lymph in the tissues of the body into the thoracic duct and then enters the blood again.]

[If peptone be injected into the lymphatic system it can be recovered unchanged. Thus the lymphatic glands have not the power to assimilate peptone and convert it into serum-albumin, as has been suggested by some observers (*Shore*).]

When the **muscles act**, not only is the lymph poured out more rapidly, but more lymph is formed. The tendons and fasciæ of the muscles of the skeleton, which are provided with numerous small stomata, absorb the lymph from the muscles. By the alternate contraction and relaxation of these fibrous structures, they act like suction-pumps, whereby the lymphatics are alternately filled and emptied, while the lymph is propelled onwards. Even **passive movements** act in the same way. If solutions be injected under the fascia lata, they may be propelled onwards to the thoracic duct by passive movements of the limb (*Ludwig, Schweigger-Seidel*).

(2) **The source of the lymph-corpuscles varies.**—(1) A very considerable number of lymph-corpuscles are derived from the **lymphatic glands** (p. 381); they are washed out of these glands into the *vas efferens* by the lymph-stream; hence, the lymph always contains more corpuscles after it has passed through a lymph-gland. Small isolated lymph-follicles permit corpuscles to pass through their limiting layer into the lymph-stream. (2) Those organs whose basis consists of **adenoid tissue** and in whose meshes numerous lymph-corpuscles occur, *e.g.*, the

mucous membrane of the entire intestinal tract, red marrow of bone, and the spleen (§ 103). The cells reach the origin of the lymph-stream by their own amœboid movements. (3) As lymph-corpuscles are returned to the blood-stream, where they appear as colourless blood-corpuscles, so they again pass out of the **blood-capillaries** into the tissues, partly owing to their amœboid movements, and they are partly expelled by the blood-pressure. In rare cases lymph-corpuscles wander from lymphatic spaces back again into the blood-vessels.

Fine particles of cinnabar or milk-globules introduced into the blood soon pass into the lymphatics. The extrusion of particles is greater during venous congestion than when the circulation is undisturbed, just as with diapedesis (§ 95); inflammatory affections of the vascular wall also favour their passage. The vessels of the portal system are especially pervious.

(4) By **mitotic division of the lymph-corpuscles** (p. 381), and also by **proliferation of the fixed connective-tissue corpuscles**. This process certainly occurs during inflammation of many organs. This has been proved for the excised cornea kept in a moist chamber; the nuclei of the cornea-corpuscles also proliferate.

That the connective-tissue corpuscles proliferate is shown by the enormous production of lymph-corpuscles in acute inflammations (with the formation of pus), *e.g.*, in extensive erysipelas, and inflammatory purulent effusions into serous cavities, where the number of corpuscles is too great to be explained by the wandering of blood-corpuscles out of the blood-vessels.

Decay of Lymph-Corpuscles.—The lymph-corpuscles disappear partly where the lymphatics arise, and also in the lymphatic glands. The presence of the fibrin-factors in the lymph—formed as they are from the breaking-up of lymph-corpuscles—seems to indicate this. In inflammation of connective-tissue, in addition to the formation of numerous new lymph-corpuscles, a considerable number seems to be dissolved; hence the lymph, and also the blood, in this case contains more fibrin. Lymph-corpuscles are also dissolved within the blood-stream, and help to form the fibrin-factors, [or rather the precursor of fibrin].

201. MOVEMENT OF CHYLE AND LYMPH.—The ultimate cause of the movement of the chyle and lymph depends upon the **difference of the pressure** at the origin of the lymphatics, and the pressure where the thoracic duct opens into the venous system.

(1) The forces which are active at the **origin of the lymphatics** are concerned in moving the lymph, but these must vary according to the place of origin—
 (a) The **lacteals** receive the first impulse towards the movements of their contents—the chyle—from the contraction of the **muscular fibres of the villi** (pp. 356, 363). When these contract and shorten, the axial lacteal is compressed, and its contents are forced in a centripetal direction towards the large lymphatic trunks. When the villi relax, the numerous valves prevent the return of the chyle into the villi.
 (b) Within those lymphatics which take the form of perivascular spaces, every time the contained *blood-vessel is dilated* the surrounding lymph will be pressed outwards.
 (c) In case of the pleural lymphatics with open mouths, every **inspiratory movement** acts like a suction-pump upon the lymph, and the same is the case with the openings or stomata of the lymphatics on the abdominal side of the *diaphragm*.
 (d) In the case of those vessels which begin by means of fine juice-canals, the movement of the lymph must largely depend upon the **tension of the juices of the parenchyma**, and this again must depend upon the tension or *pressure in the blood-capillaries*, so that the blood-pressure acts like a *vis a tergo* in the rootlets of the lymphatics.

[In some organs peculiar **pumping arrangements** are brought into action. The abdominal surface of the **central tendon** of the *diaphragm* is provided with stomata, or open communications between the peritoneal cavity and the lymphatics in the substance of the tendon. Von Recklinghausen found that milk put upon the peritoneal surface of the central tendon showed

little eddies, caused by the milk-globules passing through the stomata and entering the lymphatics. The central tendon consists of two layers of fibrous tissue arranged in different directions (fig. 277, *b*, *c*). When the diaphragm moves during respiration, these layers are alternately pressed together and pulled apart. Thus the spaces are alternately dilated and contracted, lymph being drawn into the lymphatics through the stomata (fig. 277, *h*). The same kind of pumping mechanism exists over the costal pleura. The fascia covering the muscles is another similar mechanism. The fascia consists of two layers of fibrous tissue, with intervening lymphatics (fig. 278). When a muscle contracts, lymph is forced out from between the layers of the fascia, while, when it relaxes, the lymph from the muscle, carrying with it some of the waste products of muscular action, passes out of the muscle into the fascia, between the now partially separated layers.]

[Ludwig's Experiment.

—Tie a respiration cannula in the trachea of a dead rabbit; cut across the body of the animal immediately below the diaphragm; remove the viscera, and ligature the vessels passing between the thorax and abdomen; tie the thorax to an iron ring, and hang it up with the head downwards; pour a solution of Berlin blue upon the peritoneal surface of the diaphragm; connect the respiration cannula either with a pair of bellows or an apparatus for artificial respiration, and imitate the respiratory movements. After a few minutes the lymphatics are filled with a blue injection showing a beautiful plexus.]



Fig. 277.

Section of central tendon of diaphragm. The injected lymph-spaces, *h* and *h*, are black. At *f* the walls of the space have collapsed.

(2) Within the lymph-trunks themselves, the independent contraction of their muscular fibres partly aids the lymph stream. Heller observed in the mesentery of the guinea-pig that the peristaltic movement

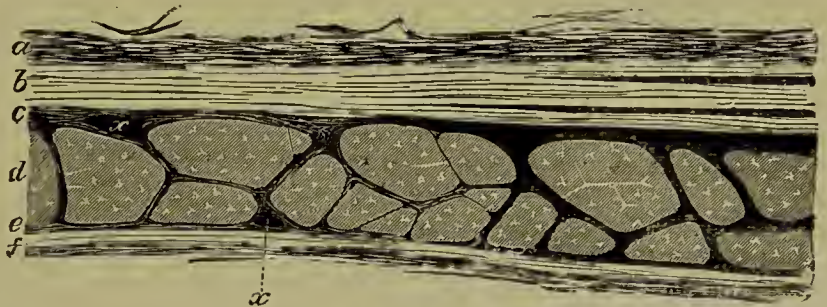


Fig. 278.

Injected lymph-spaces (black) from the fascia lata of the dog.

of the lymphatic wall passed in a centripetal direction. The numerous valves prevent any reflux. The contraction of the surrounding muscles, and pressure upon the vessels and the tissues, aid the current. If the outflow of blood from the veins is interfered with, lymph flows copiously from the corresponding tissues. [If a cannula be tied in a lymphatic of a dog, a few drops of lymph flow out at long intervals. But if even *passive* movements of the limb be made, *e.g.*, simply flexing and extending the limb, the outflow becomes very considerable and continuous.]

(3) The lymph-glands, which occur in the course of the lymphatics, offer very considerable resistance to the lymph-stream, which must pass through the lymph-paths, whose spaces are traversed by adenoid tissue, and contain a few lymph-corpuscles. But this is, to a certain extent, compensated for by the non-striped muscle which exists in the capsule and trabeculae of the glands. When they contract they force on the lymph, while the valves prevent its reflux. Enlarged lymphatic glands have been seen to contract when stimulated electrically. [Botkin has stimulated enlarged lymphatic glands with electricity in cases of leukaemia, and found that they contracted somewhat.]

(4) The lymph-vessels gradually join to form larger vessels, and finally end in

one trunk. Thus the *sectional area* diminishes, so that the **velocity** of the current and the pressure are increased. Nevertheless, the velocity is always small; it varied from 230 to 300 millimetres per minute in the large lymphatic in the neck of a horse, a fact which enables us to conclude that the movement must be very slow in small vessels. The **lateral pressure** at the same place was 10 to 20 mm., and in the dog 5 to 10 mm. of a weak solution of soda, although it was = 12 mm. Hg in the thoracic duct of a horse.

(5) The **respiratory movements** exercise a considerable influence upon the lymph-stream in the thoracic duct, and in the right lymphatic duct; every inspiration favours the passage of the venous blood, and also of the lymph towards the heart; indeed, the pressure in the thoracic duct may even become negative. [The *diastolic suction of the heart*, by diminishing the pressure in the subclavian vein, also favours the inflow of lymph into the thorax.]

(6) **Lymph-hearts** exist in certain cold-blooded animals. The frog has two **axillary hearts** (above the shoulder near the vertebral column), and two **sacral hearts**, one on each side of the coccyx near the anus (fig. 279, L). They beat, but not synchronously, about sixty times per minute, and contain 10 cubic millimetres of lymph.

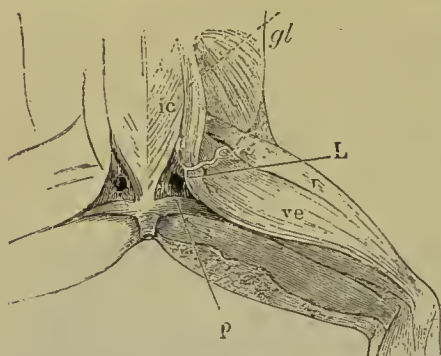


Fig. 279.

Posterior pair of lymph-hearts (L) of the frog.

They have transversely-stripped muscular fibres in their walls, and are also provided with *nerve-ganglia*. The posterior pair pump the lymph into the branch of the vena iliaca communicans, and the anterior pair into the vena sub-scapularis. Their pulsation depends partly, but not exclusively, upon the spinal cord, for if the cord be rapidly destroyed, they may cease to pulsate, but not unfrequently they continue to pulsate after removal of the cord. [If the cord, however, be destroyed gradually, they continue to beat (*Kabrhel*).] A second source of their pulsatile movements is to be sought for in Waldeyer's ganglia. Stimulation of the skin, intestine, or blood-heart influences them reflexly—partly accelerating and partly retarding them, [most frequently arresting them in diastole, so that there seems to be an inhibitory mechanism in the cord, but it is not affected by atropine (*Kabrhel*).] If the coccygeal nerve, which connects the sacral hearts to the spinal

cord, be divided, these effects do not occur. *Strychnia* accelerates their movements, and so does heating of the spinal cord; but if the cord be cooled, they are retarded. A lymph-heart arrested by being exposed, or after the action of muscarin, can be caused to beat by filling it under pressure, but this is not the case when the arrest is caused by destruction of its nerves. *Antiarin* paralyses the lymph-heart and the blood-heart at the same time, while *curare* paralyses the former alone. In other amphibians there are two lymph-hearts; in the ostrich and cassowary and some swimming birds, and in the embryo chick 1 or 2. They occur in some fishes, *e.g.*, near the caudal vein of the eel.

(7) The **nervous system** has a direct effect upon the lymph-stream, on account of its connection with the muscles of the lymphatics and lymph-glands, and with the lymph-hearts where these exist. Kühne observed that the cornea corpuscles contracted when the corneal nerves were stimulated, [and Hoffman has described the termination of nerves in connective-tissue corpuscles.] Goltz also observed that when a dilute solution of common salt was injected under the skin of a frog, it was rapidly absorbed, but if the central nervous system had been destroyed, it was not absorbed.

If **inflammation** be produced in the hind legs of a dog, and if the sciatic nerve be divided on one side, oedema and a simultaneous increase of the lymph-stream occur on that side. [A combination of congestion and inflammation greatly increases the lymph-stream, and this is still more the case when the nerves are divided at the same time.]

Ligature the leg of a frog, except the nerves, so as to arrest the circulation, and place the leg in water; it swells up very rapidly, but a dead limb does not swell up. So that absorption is independent of the continuance of the circulation. Section of the sciatic nerve, or destruction of the spinal cord (but not section of the brain), arrests absorption.

202. ABSORPTION OF PARENCHYMATOUS EFFUSIONS.—Fluids which

pass from the blood-vessels into the spaces in the tissues, or those injected subcutaneously, are absorbed chiefly by the blood-vessels but also by the lymphatics. Small particles, as after tattooing with cinnabar or China ink, may pass from the tissue-spaces into the lymphatics—and so do blood-corpuscles from extravasations of blood, and fat-granules from the marrow of a broken bone. If all the lymphatics of a part are ligatured, absorption takes place quite as rapidly as before; hence, absorbed fluid must pass through the thin membranes of the blood-vessels. The corresponding experiment of ligaturing all the blood-vessels, when no absorption of the parenchymatous juices take place, does not prove that the lymphatics are not concerned in absorption, for, after ligaturing the blood-vessels of a part, of course the formation of lymph, and also the lymph-stream, must cease. When fluids are injected under the skin, absorption takes place very rapidly—more rapidly than when the substance is given by the mouth. The **subcutaneous injection** of drugs is extensively used, but of course the substances used must not corrode, irritate, or coagulate the tissues.

Some substances do not act when given by the mouth, as snake poison, poisons from dead bodies, or putrid things, although they act rapidly when introduced subcutaneously. If **emulsin** be given by the mouth, and **amygdalin** be injected into the veins of an animal, hydrocyanic acid is not formed, as the emulsin seems to be destroyed in the alimentary canal. If the emulsin, however, be injected into the blood, and the amygdalin be given by the mouth, the animal is rapidly poisoned, owing to the formation of hydrocyanic acid, as the amygdalin is rapidly absorbed from the intestinal canal. The amygdalin, a glucoside ($C_{20}H_{27}NO_{11}$), is acted upon by fresh emulsin like a ferment; it takes up $2(H_2O)$ and yields hydrocyanic acid (HCN), + oil of bitter almonds (C_7H_6O), + sugar $2(C_6H_{12}O_6)$. Serum injected subcutaneously is rapidly absorbed; it is decomposed within the blood-stream, and increases the amount of urea. Albuminous solutions, oil, peptones, and sugars are also absorbed.

203. OEDEMA, DROPSY, AND SEROUS EFFUSIONS.—[**Dropsy.**—As aptly illustrated by Lauder Brunton, the lymph-spaces may be represented by eisterns, each of which is provided with supply pipes—the arteries and capillaries; while there are two exit pipes—the veins and lymphatics. In health, the balance between the inflow and outflow is such that the spaces are merely moistened with fluid. When a cannula is placed in a lymphatic vessel in a dog, only a few drops of lymph flow out at long intervals, but if the veins of the limb be ligatured, the lymph flows much more quickly. This is in part due to the increased transudation of fluid from the small blood-vessels, but it may also be due to fluid passing away by the lymphatics when it can no longer be carried away by the veins. We cannot say what is the relative share of the veins and the lymphatics, nor in the above experiment do we know how much is due to increased transudation or diminished absorption. When there is an undue accumulation of fluid more or less like serum in the lymph-spaces, we have the condition termed **dropsy**. When there is general dropsy it is called **anasarca**.]

Oedema.—If the efferent veins and lymphatics of an organ be ligatured, or if resistance be offered to the outflow of their contents, congestion and a copious transudation of lymph into the tissue take place. These are most marked in the skin and subcutaneous cellular tissue. The soft parts swell up, without pain or redness, and a doughy swelling, which **pits on pressure** with the finger, results. These are the signs of lymph-congestion, which is called **oedema** when the fluid is *watery* and localised.

Under similar circumstances lymph is effused into the **serous cavities**. [In the peritoneum it is **ascites**—thorax, **hydro-thorax**—pericardium, **hydro-pericardium**—cranium, **hydrocephalus**—tunica vaginalis, **hydrocele**—joints, **hydrarthrosis**, &c.] If, at the same time, a large number of colourless blood-corpuscles pass out of the blood-vessels into the cavity, the fluid becomes more and more like pus. In order that these corpuscles may proliferate, a considerable percentage of albumin is necessary. When the pressure within the serous cavity rises above that in the small blood-vessels, water may pass into the blood. These sero-purulent effusions not unfrequently undergo changes, and yield decomposition-products, such as leucin, tyrosin, xanthin, kreatin, kreatinin (?), uric acid (?), urea. Endothelium from the serous cavity, sugar in pleuritic effusions and in oedemas with little albumin, cholesterolin frequently in hydrocele fluid, and succinic acid in the fluid of echinococci have all been found in these effusions. The effusion of lymph may arise not only from pressure upon the lymphatics, but also from inflammation and thrombosis of the lymphatics themselves, in which cases not unfrequently new lymphatics are formed, so that the communication is re-established. Sometimes the ductus thoracicus bursts and lymph is poured directly into the abdomen or thorax. [Ligature of the thoracic duct results in rupture of the receptaculum chyli and escape of chyle and lymph into the large serous cavities (*Ludwig*).]

When dropsy or effusion of fluids occurs into serous cavities, there is always a greater transudation of fluid through the blood-vessels. The abdominal blood-vessels, and those which yield a watery effusion under normal circumstances, are those most liable to be affected.

Transudation is favoured by—(1) **Venous congestion**, so as to raise the blood-pressure, in which case the effusion usually contains little albumin and few lymph-corpuscles, while the coloured corpuscles, on the contrary, are more numerous the greater the venous obstruction. Ranvier produced œdema artificially by ligaturing the vena cava in a dog, and at the same time dividing the sciatic nerve. The paralytic dilatation of the blood-vessels thereby produced caused an increased amount of blood to pass to the limb, while the blood-pressure was raised, and both factors favoured the transudation of fluid. [Ranvier's experiment proves that mere ligature of the venous trunk of a limb *by itself* is not sufficient to cause œdema. The œdema is due to the concomitant paralysis of the vaso-motor nerves. If the motor roots of the sciatic nerve alone be divided along with ligature of the vena cava, no œdema occurs, but if the vaso-motor fibres are divided at the same time, the limb rapidly becomes œdematous. There is such an increased transudation through the vascular walls that the veins and lymphatics cannot remove it with sufficient rapidity, and œdema occurs. If there be weakness of the vaso-motor nerves, slight obstruction is sufficient to produce œdema.] When the leg-veins are occluded with an injection of gypsum, œdema occurs. (2) Some unknown **physical changes** occur in the **protoplasm** of the endothelium of the capillaries and blood-vessels, which favour the transudation of albumin, hæmoglobin, and even blood-corpuscles. This occurs when abnormal substances accumulate in the blood—*e.g.*, dissolved hæmoglobin—and when the blood contains little O or albumin. The same has been observed after exposure to too high temperatures, and the swelling of soft parts in the neighbourhood of an inflammatory focus seems due to the transudation of fluid through the altered vascular wall. It is probable that a nervous influence may affect particular areas through its action on the blood-vessels of the part (it may be upon the protoplasm of the blood-capillaries). The transudations of this nature usually contain much albumin and many lymph-corpuscles. (3) When the blood contains a very large amount of water, the tendency to transudation of fluid is increased. After a time it may produce the changes indicated in (2), and when long continued may increase the permeability of the vascular wall. Watery lymphatic effusions from watery blood—“**cachectic œdema**”—occur in feeble and badly-nourished individuals. [One of the commonest forms of dropsy is the slight œdema of the legs in anæmic persons, in whom the heart and lungs are healthy. Many factors are involved—the blood-pressure, watery condition of the blood, the condition of nutrition of the capillaries, and probably a tendency to vaso-motor paresis (*Brunton*).]

[The fluid poured out varies according to the rapidity with which this occurs. In acute inflammations effusion or **exudation** takes place rapidly, and the fluid contains the precursor of fibrin, so that it tends to coagulate spontaneously. There is every gradation between the non-coagulable hydrocele fluid and the coagulable exudation in inflammation. The fluids in different dropsies vary in composition, and some have more cells in them, depending on local causes, as in some situations absorption is more active than in others. The pleural fluid contains most solids, then ascitic, cerebro-spinal, and, lastly, that in the subcutaneous tissue. Transudation corresponds to the process of filtration through animal membranes; *i.e.*, the transudation contains only those substances already present in the blood-plasma. The filtrate may even contain more salts than the original fluid, as is often the case with fluids containing crystalloid and colloid bodies. Senator finds, in cases of œdema of the leg, that increase of the venous pressure increases the proteids in the transudation, but causes no essential change in the amount of the salts.]

[(4) Ostroumoff found that stimulation of the lingual nerve not only causes the blood-vessels of the tongue to dilate, but that the corresponding side of the tongue becomes œdematous. If a solution of dilute hydrochloric acid or quinine (§ 145) be injected into the duct of the sub-maxillary gland, and the chorda tympani stimulated, there is no secretion of saliva, but the gland becomes œdematous. In an animal poisoned with atropin, stimulation of the chorda causes dilatation of the blood-vessels, although there is no secretion of saliva, nevertheless the gland does not become œdematous (*Heidenhain*). As Brunton suggests, this experiment points to some action of atropin on the blood-vessels which has hitherto been entirely overlooked.]

204. COMPARATIVE PHYSIOLOGY.—In the frog large lymph-sacs, lined with endothelium, exist under the skin, while large lymph-sacs lie in relation with the vertebral column—one on each side—separated from the abdominal cavity by a thin membrane, perforated with stomata. This is the **cysterna lymphatica magna** of Panizza. Some amphibians and many reptiles have under the skin large lymph-spaces, which occupy the whole of the dorsal region of the body. All reptiles and the tailed amphibians have large elongated reservoirs for lymph along the course of the aorta. The lymph-apparatus of the tortoise (fig. 270) is very extensive. The osseous fishes have in the lateral parts of their backs an elongated lymph-trunk, which reaches from the tail to the anterior fins, and is connected with the dilated lymphatic rootlets in the base of the tail and in the fins. The largest internal lymph-sinus is in the region of the œsophagus. Many birds possess a sinus-like dilatation or lymph-space in the region of the

tail. The lymph-spaces communicate with the venous system—with valves properly arranged—usually in connection with the upper vena cava. Lymph-hearts have already been referred to (§ 201, 6). In *carnivora* the lymph-glands of the mesentery are united into one large compact mass, the so-called “pancreas Asellii.”

205. HISTORICAL.—Although the Hippocratic School was acquainted with the lymph-glands from their becoming swollen from time to time, and although Herophilus and Erasistratus had seen the mesenteric glands, yet Aselli (1662) was the first who accurately described the lacteals of the mesentery with their valves. Pecquet (1648) discovered the receptaculum chyli; Rudbeek and Thom. Bartholinus the lymphatic vessels (1650–52); Eustachius (1563) was acquainted with the thoracic duct, which Gassendus (1654) maintained that he was the first to see; Lister noticed that the chyle became blue when indigo was injected into the intestine (1671); Sömmerring observed the separation of fibrin when lymph coagulated; Reuss and Emmert discovered the lymph-corpuscles. The chemical investigations date from the first quarter of this century; they were carried out by Lassaigne, Tiedemann, Gmelin, and others. The two last-named observers noticed that the white colour of chyle was due to the presence of fatty granules.

Physiology of Animal Heat.

206. SOURCES OF HEAT.—The heat of the body is an uninterrupted evolution of kinetic energy, which we must represent to ourselves as due to vibrations of the corporeal atoms. The **ultimate source** of the heat is contained in the potential energy taken into the body with the food, and with the O of the air absorbed during respiration. The **amount** of heat formed depends upon the amount of energy liberated.

The energy of the food-stuffs may be called “**latent heat**,” if we assume that when they are used up in the body, chiefly by a process of combustion, kinetic energy is liberated only in the form of heat. As a matter of fact, however, mechanical energy and electrical energy are developed from the potential energy. In order to obtain a unit-measure for the energy liberated, it is advisable to express all the potential energy as **heat-units**.

Calorimeter.—This instrument enables us to transform the potential energy of the food into heat, and, at the same time, to measure the number of heat-units produced.

Favre and Silbermann used a **water-calorimeter** (fig. 280). The substance to be burned is placed in a large cylindrical combustion-chamber (K), suspended in a large cylindrical vessel (L) filled with water (w), so that the combustion-chamber is completely surrounded by the water. Three tubes open into the upper part of the chamber; one of them (O) supplies the air which is necessary for combustion, it reaches almost to the bottom of the chamber; the second (a) is fixed in the middle of the lid, and is closed above with a thick glass plate, and on this is placed, at an angle, a small mirror (s), which enables

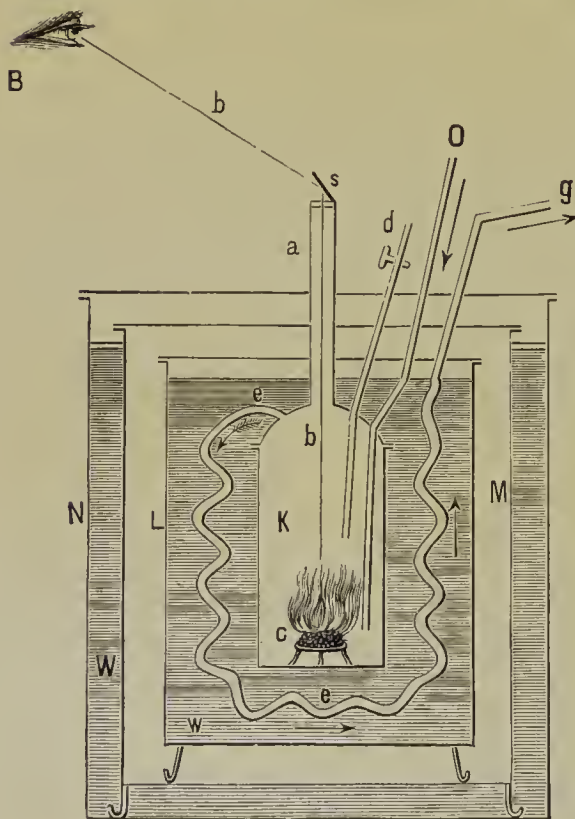


Fig. 280.

Water-calorimeter of Favre and Silbermann.

an observer to look into the chamber, and observe the process of combustion at *c*. The third tube (*d*) is used only when combustible gases are to be burned in the chamber. It can be closed by means of a stop-cock. A lead tube (*e, e*), with many twists, passes from the upper

part of the chamber through the water, and finally opens at *g*. The gaseous products of combustion pass out through this tube, and in doing so help to heat the water. The cylindrical vessel with the water is closed with a lid which transmits the four tubes. The water-cylinder stands on four feet within a large cylinder (M), which is filled with some good non-conductor of heat, and this again is placed in a large vessel filled with water (W). This is to prevent any heat reaching the inner cylinder from without. A weighed quantity of the substance (*c*) to be investigated is placed in the combustion-chamber. When combustion is ended, during which the inner water must be repeatedly stirred, the temperature of the water is ascertained by means of a delicate thermometer. If the increase of the temperature and the amount of water are known, then it is easy to calculate the number of **heat-units** produced by the combustion of a known weight of the substance (see *Introduction*).

The **ice-calorimeter** may also be used. The inner cylinder is filled with ice and not with water, and ice is also placed in the outer cylinder to prevent any heat from without from acting upon the inner ice. The heat given off from the combustion-chamber causes a certain amount of the ice to melt, and the water thereby produced is collected and measured. It requires 79 heat-units to melt 1 grm. of ice to 1 grm. of water at 0° C.

[The amount of heat produced by a **living animal** is similarly measured. The animal (fig. 281), in a cage, is placed in a large vessel, which is placed within another vessel, and the interspace filled with water. The whole should be enclosed in a large box packed with fur, shavings, feathers, or other bad conductor of heat. A tube, D, opens into the inner space, and from it there is an exit-tube, D', which winds many times in the water-space beneath. Air passes in through D and out by D'. The temperature of the water is ascertained by thermometers T and T', while the water

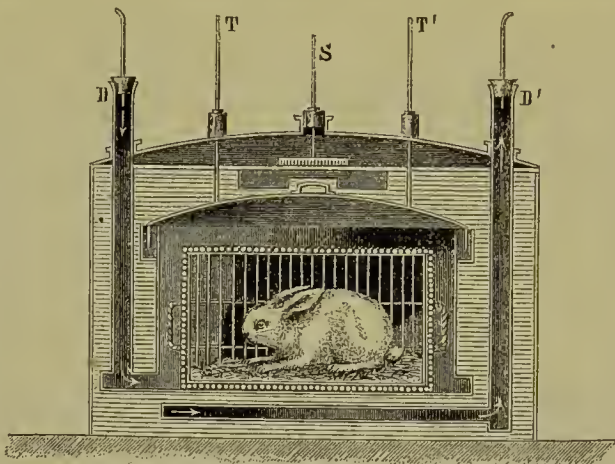


Fig. 281.

Water-calorimeter of Dulong.

is moved by a stirrer (S) placed between the two. In **Rosenthal's calorimeter**, one cylinder, surrounded by an air-jacket, is placed inside another, and the animal is placed in the inner cylinder.]

Just as in a calorimeter, although *much more slowly*, the food-stuffs within our body are burned up, oxygen being supplied, and thus potential energy is transformed into kinetic energy, which, in the case of a person at *rest*, almost completely appears in the form of heat.

Heat-Units.—Favre, Silbermann, Frankland, Rechenberg, B. Danilewsky, and others have made calorimetric experiments on the heat produced by food. According to Danilewsky, 1 gram of the following dry substances yields heat-units :—

Casein, . . . 5855	Palmitin, . . 8883	Cow's milk, 5733	Maize, . . . 5188
Fibrin, . . . 5772	Olein, . . . 8958	Woman's milk, . 4837	Alcohol, . . 6980
Peptone, . . 4876	Stearin, . . 9036	Egg-yolk, . . 4479	Urea, . . . 2537
Glutin, . . . 5493	Ox-fat, . . . 9686	Potatoes, . . 4234	Muscle } 4400
Ox-blood, . . 5900	Glycerin, . . 4179	Rye-bread, 4471	Extractives } (Liebig's)
Ox-flesh, . . 5724	Starch, . . . 4479	Wheat-bread, 4351	Flesh extract, 3216
Vegetable fibrin, . 6231	Dextrose, . . 3939	Rice, . . . 4806	Acetic acid, . 3318
Ghltin, . . . 6141	Maltose, . . 4163	Peas, . . . 4889	Butyric acid, 5647
Legumin, . . 5573	Milk-sugar, 4162	Buck-wheat, 4288	Palmitic acid, 9316
	Cane-sugar, 4173		

As albumin is only oxidised to the stage of urea, we must deduct the heat-units obtainable from urea from those of albumin, and as 1 part of albumin yields in round numbers about $\frac{1}{3}$ of urea, we obtain about 5100 calories (=2170 kilogram-metres) for 1 grm. of albumin.

Isodynamic foods, *i.e.*, those that produce an equal amount of heat; 100 grms. animal albumin (after deducting the heat-units of urea)=52 fat=114 starch=129 dextrose; 100 grms. fat are isodynamic with 243 dry flesh or 225 of dry syntonin (*Rubner*); 100 grms. of vegetable albumin=55 fat=121 starch=137 dextrose (*Danilewsky*). *Rubner* calculated that in man, with a mixed diet, the *available* heat-units for 1 grm. of albumin=4100; 1 grm. fat=9300; and for 1 grm. carbohydrate=4100 calories.

When we know the weight of any of the above-named substances consumed by a man in twenty-four hours, a simple calculation enables us to determine how many heat-units are formed in the body by oxidation, *i.e.*, provided the substance is completely oxidised.

[Several sources of heat-production or thermogenesis are to be found in all tissues wherever oxidation is going on. The metabolism of protoplasm is always associated with the evolution of heat.]

(1) *In the transformation of the chemical constituent of the food, endowed with a large amount of potential energy into such substances as have little or no energy.* The organic substances used as food consist of C, H, O, N, so that there takes place—(a) **Combustion** of C into CO_2 , of H into H_2O , whereby heat is produced; 1 gm. C burned to produce CO_2 yields 8080 heat-units, while 1 gm. H oxidised to H_2O yields 34,460 heat-units. The O necessary for these purposes is absorbed during respiration, so that, to a certain extent at least, the amount of heat produced may be estimated from the amount of O consumed. The same consumption of O gives rise to the same amount of heat whether it is used to oxidise H or C (*Pflüger*). There is a relation, amounting to cause and effect, between the amount of heat produced in the body and the O consumed. The cold-blooded animals, which consume little O, have a low temperature; amongst warm-blooded animals, 1 kilo. of a living rabbit takes up within an hour 0.914 gm. O, and its body is heated to a mean of 38°C . 1 kilo. of a living fowl uses 1.186 grms. O, and gives a mean temperature of 43.9°C . The amount of heat produced is the same whether the combustion occurs slowly or quickly; the rapidity of the metabolism, therefore, affects the rapidity, but not the absolute amount of heat-production. The combustion of inorganic substances in the body, *e.g.*, of the sulphur into sulphuric acid, the phosphorus into phosphoric acid, is another, although very small, source of heat.

[The **muscles** form about the half of the whole mass of the body and the bones nearly the other half. In the latter, oxidation does not go on actively, so that the muscles must be the great seats of heat-production or thermogenesis in the body. This view is supported by the fact that the blood leaving a muscle at rest contains more CO_2 than the blood in the right ventricle. Muscular exercise greatly increases the metabolism and the CO_2 excreted (§ 126), but at the same time, there is a great increase in heat-production. The muscles, therefore, are the great thermogenic tissues, and they yield $\frac{4}{5}$ ths of the heat in health. The several **secreting glands**, especially the liver and the alimentary canal, during digestion, are also foci of heat-formation.]

(b) In addition to the processes of combustion or oxidation, all those **chemical processes** in our body, by which the amount of the available potential energy which is present is diminished, in consequence of a greater satisfaction of atomic affinities, lead to the production of heat. In all cases where the atoms assume more stable positions with their affinities satisfied, chemical energy passes into kinetic thermal energy, as in the alcoholic fermentation of grape-sugar, and other similar processes.

Heat is also developed during the following chemical processes:—

(a) During the union of bases with acids. The nature of the base determines the amount of heat produced, while the nature of the acid is without effect. Only in those cases where the acid, *e.g.*, CO_2 , is unable to neutralise the alkaline reaction, the amount of heat produced is less. The formation of compounds of chlorine (*e.g.*, in the stomach) produces heat.

(b) When a neutral salt is changed into a basic one. In the blood the sulphuric and phosphoric-acids derived from the combustion of S and P are united with the alkalis of the blood to form basic salts. The decomposition of the carbonates of the blood by lactic and phosphoric acids form a double source of heat, on the one hand, by the formation of a new salt, and, on the other, by the liberation of CO_2 , which is partly absorbed by the blood.

(c) The combination of hæmoglobin with O (§ 36).

During those chemical processes, whereby the heat of the body is produced, heat-absorbing intermediate compounds are not unfrequently formed. Thus, in order that the final stage of more complete saturation of the affinities be reached, intermediary atomic groups are formed, whereby heat is absorbed. Heat is also absorbed when the solid aggregate condition is changed during retrogressive processes. But these intermediary processes, whereby heat is lost, are very small compared with the amount of heat liberated when the end-products are formed.

(2) Certain **physical processes** are also a source of heat.—(a) The **transformation of the kinetic mechanical energy** of internal organs, when the work done is not transferred outside the body, produces heat. Thus the whole of the kinetic energy of the heart is changed into heat, owing to the resistance opposed to the blood-stream (§ 93). The same is true of the mechanical energy evolved by many muscular viscera. The torsion of the costal cartilages, the friction of the current of air in the respiratory organs, and the ingesta in the digestive tract, all yield heat.

An excessively minute amount of the mechanical energy of the heart is transferred to surrounding bodies by the cardiac impulse and the superficial pulse-beats, but this is infinitesimally small. During respiration, when the respiratory gases and other substances are expired, a very small amount of energy disappears externally, which does not become changed into heat. If we assume that the daily work of the circulation exceeds 86,000 kilogram-metres, the heat evolved is equal to 204,000 calories in twenty-four hours (§ 93), which is sufficient to raise the temperature of a person of medium size 2°C .

(b) When, owing to muscular activity, the body produces work which is transferred to external objects, *e.g.*, when a man ascends a tower or mountain, or throws a heavy weight, a portion of the kinetic energy passes into heat, owing to friction of the muscles, tendons, and the articular surfaces, as well as to the shock and pressure of the ends of the bones against each other.

(c) The electrical currents which occur in muscles, nerves, and glands very probably are changed into heat. The chemical processes which produce heat evolve electricity, which is also changed into heat. This source of heat, however, is *very small*.

(d) Other processes are the formation of heat from the *absorption of CO_2* , by the *concentration of water* as it passes through membranes, in *imbibition*, and the *formation of the solids*, *e.g.*, of chalk in the bones. After death, and in some pathological processes during life, the *coagulation of blood* and the production of *rigor mortis* are sources of heat.

207. HOMOIOTHERMAL AND POIKILOTHERMAL ANIMALS.—In place of the old classification of animals into “cold-blooded” and “warm-blooded,” another basis of classification seems desirable, *viz.*, the relation of the temperature of the body to the temperature of the surrounding medium. Bergmann introduced the word **homoiothermal** for the **warm-blooded** animals (mammals and birds), because these animals can maintain a very uniform temperature, even although the surrounding temperature be subject to considerable variations. The so-called **cold-blooded** animals are called **poikilothermal**, because the temperature of their bodies rises or falls, within wide limits, with the heat of the surrounding medium.

When **homoiothermal animals** are kept for a long time in a cold medium, their heat-production is increased, and when they are kept for a long time in a warm medium it is diminished.

Fordyce gave a proof of the nearly uniform temperature in man. A man remained ten minutes in an oven containing very dry hot air (§ 218), and yet the temperature of the palm of his hand, mouth, and urine was increased only a few tenths of a degree. Beequerel and Breehet investigated the temperature of the human biceps (by means of thermo-electric needles), when the arm has been one hour in iced water, and yet the temperature of the muscular tissue was cooled only 0.2°C . The same muscle did not undergo any increase in temperature, or at most 0.2°C , when the man's arm was placed for a quarter of an hour in water at 42°C .

If heat be rapidly abstracted (§ 225) or rapidly supplied (§ 221) to the body, so as to produce rapid variation of the temperature, life is endangered.

Poikilothermal animals behave very differently; the temperature of their bodies generally follows, although with considerable variations, the temperature of the surroundings. When the temperature of the surroundings is increased, the amount of heat produced is increased, and when the surrounding temperature falls, the amount of heat evolved within the body also falls.

The following table shows very clearly the characters of **poikilothermal animals**, *e.g.*, frogs which were placed in air and water of varying temperatures. They were immersed up to the mouth. The temperature was measured by means of a thermometer introduced through the mouth into the stomach.

In Water.		In Air.	
Temperature of the Water.	Temperature of Frog's Stomach.	Temperature of the Air.	Temperature of Frog's Stomach.
41·0° C.	38·0° C.	40·4° C.	31·7° C.
30·0	29·6	27·4	19·7
20·6	20·7	16·4	14·6
5·9	8·0	6·2	7·6
2·8	5·3	5·9	8·6

[Temperature of Different Animals.

Birds.		Mammals.		Temp.	
	Temp.				Temp.
Thalassidroma,	40·30	Swallow,	44·03	Panther,	38·90
Procellaria,	40·80	Gull,	37·8	Mouse,	41·1
Goose,	41·70			Dolphin,	35·5
Sparrow,	{ 39·08	Tiger,	37·20	Sheep,	{ 37·30-40·00
Pigeon,	41·80-42·50	Horse,	36·80-37·50		{ 39·50-40·00
Turkey,	42·70	Rat,	38·80		{ 40·00-40·50
Guinea-fowl,	43·90	Hare,	37·80	Ape,	35·50
Duck,	{ 43·90	Cat,	38·30-38·90	Guinea-pig,	35·76-38·00
Crow,	41·17	Guinea-pig,	38·80	Rabbit,	37·50-38·00
		Dog,	{ 37·40	Ox,	37·50
			{ 39·00	Ass,	36·95
			{ 39·60	[Gavarret & Rosenthal].]	

Reptiles—Snakes, 10°–12°, but higher when incubating. *Amphibians and fishes*—0·5°–3° above the temperature of the surroundings. *Arthropoda*—0·1°–5·8° above the surroundings. Bees in a hive, 30°–32°, and when swarming, 40°. The following animals have a temperature higher than the surrounding temperature :—Cephalopods, 0·57°; molluscs, 0·46°; echinoderms, 0·40°; medusæ, 0·27°; polyps, 0·21° C.

208. ESTIMATION OF TEMPERATURE.—By using thermometric apparatus, we are enabled to obtain information regarding the degree of heat of the body to be investigated. For this purpose the following methods are employed :—

A. The Thermometer.—Celsius (1701–1744) divided his thermometer into 100 parts, and each part was again divided into 10 parts, so that $\frac{1}{100}$ ° C. could be easily read off. All thermometers which have been used for a long time give too high readings, hence they should be compared, from time to time, with a normal thermometer. When taking the temperature, the bulb ought to be surrounded for fifteen minutes, and during the last five minutes the mercury column ought not to vary. A very sensitive thermometer will indicate the temperature after seven seconds if the urine stream be directed upon its bulb. **Minimal** and **maximal** thermometers are often of use to the physician.

[Clinically, one of the thermometers shown in fig. 282 may be used. They are self-registering maximum thermometers, *i.e.*, a portion of the mercury is separated from the mercurial column, to form the index, the top of which indicates the temperature. Before being used, the index must be well below the normal temperature. Various forms of surface thermometers have been used.]

Walferdin's metastatic thermometer (fig. 283) is specially useful for comparative observation. The tube is very narrow in comparison with the bulb, and in order that the stem be not too long, it is constructed so that the amount of mercury can be varied. A quantity of mercury is

taken, so that with the temperature expected the thread of mercury will stand about the middle of the stem. A small bulb at the upper part of the stem receives the ex-

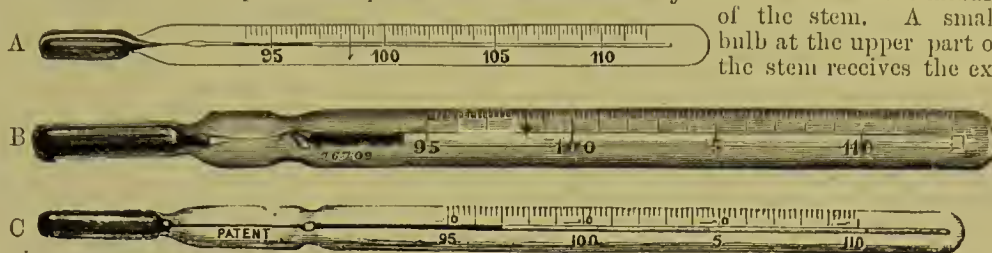


Fig. 282.

A, Casella's "infallible," B, "Ferris' perfect," and C, Evans' and Wormull's "standard" clinical thermometers.

cess of Hg. Suppose a temperature between 37° – 40° C. is to be measured, the bulb is first heated a little over 40° C., it is then suddenly cooled, and shaken at the same

time, so that the thread of mercury is thereby suddenly broken above 40° . The tube is so narrow that 1° C. is equal to about 10 centimetres of the length of the tube, so that $\frac{1}{100}^{\circ}$ C. is still 1 millimetre in length. The scale is divided empirically, but the value of the divisions must be compared with a normal thermometer.

Kronecker and Meyer used very small maximal "outflow thermometers," and caused them to pass through the intestinal canal, or through large blood-vessels. The mercury flows out of the short open tube, and of course more flows out the higher the temperature. After these small bulbs have passed through the animal, a comparison is instituted with a normal thermometer, to determine at what temperature the mercury reaches the free margin of the tube.

B. Thermo - electric Method.—This method enables us to determine the temperature accurately and rapidly (fig. 284, I). The thermo-electric galvanometer of Meissner and Meyerstein consists of a circular magnet (*m*), suspended by a thread of silk (*c*), to which a small mirror (*S*) is attached. A large stationary bar magnet (*M*) is placed near the

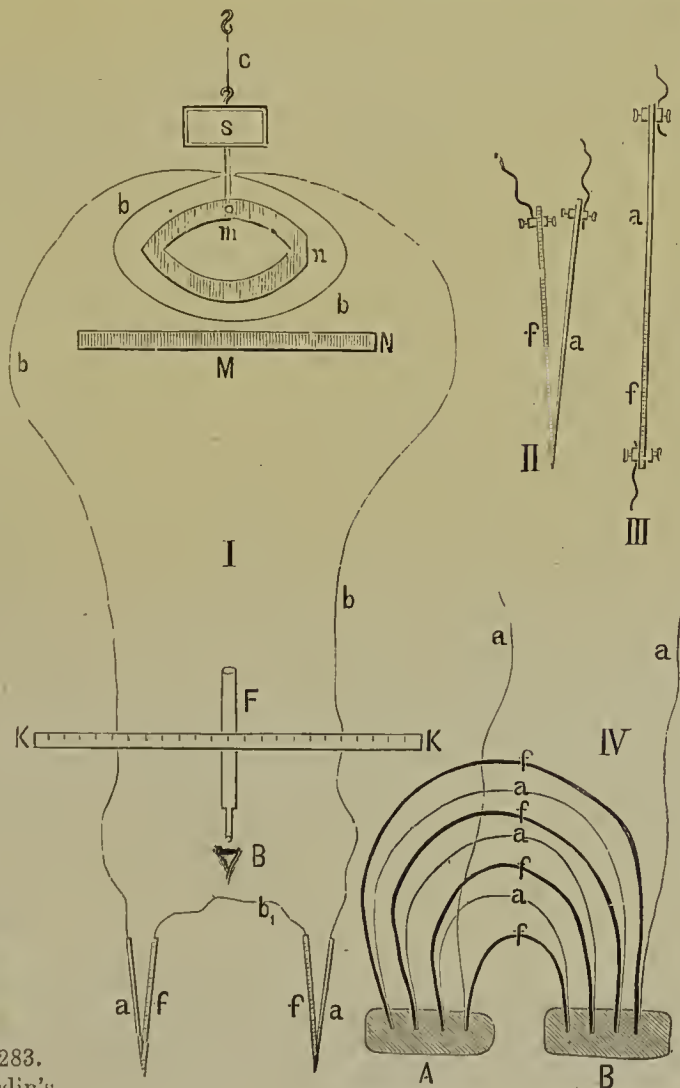


Fig. 283.
Walferdin's
metastatic
thermo-
meter.

Fig. 284.

Scheme of thermo-electric arrangements for estimating the temperature.

magnet (*m*), so that the north poles (*n* and *N*) of both magnets point in the same direction, and

it is so arranged that the suspended magnet is caused to point to the north by a minimal action of M . A thick copper wire (b, b) is coiled several times round m (although in the fig. it is represented as a single coil), and the ends of the wire are soldered to two thermo-elements, each composed of two different metals—iron and German silver, the two similar free elements being united by a wire (b_1), so that the two thermo-elements form part of a closed circuit. A horizontal scale (K, K) is placed at a distance of 3 metres from the mirror, so that the divisions of the scale are seen in the mirror. The scale itself rests upon a telescope (F) directed towards the mirror. The observer (B), who looks through the telescope, can see the divisions of the scale in the mirror. When the magnet, and with it the mirror, swing out of the magnetic meridian, the observer notices other divisions of the scale in the mirror. When one of the thermo-elements is heated, an electrical current is produced, which passes from the iron to the German silver in the heated couple, and causes a deviation of the suspended magnet. Suppose a person were swimming in the direction of the current in the conducting wire, then the north pole of the magnet moves to the north (*Ampère*). The tangent of the angle ϕ , through which the freely movable magnet is diverted by a galvanic current, from its position of rest or zero, in the magnetic meridian, is the same as the galvanic stream; G is proportional to the magnetic energy D , *i.e.*, $\text{tang. } \phi = \frac{G}{D}$. If G is to remain the same, and the $\text{tang. } \phi$ to be as large as possible,

the magnetic energy must be diminished as much as possible. If the magnetism of the suspended magnet be indicated by m , and that of the earth by T , the magnetic directing energy $D = Tm$, so that D can be distinguished in two ways: (1) by diminishing the magnetic moment of the suspended magnet, as may be done by using a pair of astatic needles, such as are used in Nobili's galvanometer; (2) and also by weakening the magnetism of the earth, by placing an accessory stationary magnet (Hauy's rod) in the same direction, and near the suspended magnet. An important arrangement for rapidly getting the magnet to zero is the dead-beat arrangement of Gauss (not figured in the scheme). It consists of a thick copper cylinder, on which the wire of the coil is wound. This mass of copper may be regarded as a closed multiplier with a very large transverse section. The vibrating magnet induces in this closed circuit a current of electricity, whose intensity is greatest when the velocity of the excursion of the magnet is greatest, and which takes the opposite direction as soon as the magnet returns towards zero. These induced currents cause a diminution of the vibrations of the magnet in this way, that the arc of vibration of the magnet diminishes very rapidly, almost in a geometrical progression. The induced damping-current is stronger, the less the resistance in the closed circuit, and in the damper or dead-beat arrangement itself, the greater the section of the copper ring. This damping arrangement limits the oscillations of the magnet, and it comes to rest rapidly and promptly after 3 or 4 small vibrations, so that much time is saved. The angle of deviation is so small that the angle itself may be taken instead of the tangent.

The thermo-electric needles of Dutochet (fig. 284, II) may be placed in the circuit. They consist of iron and German silver soldered at their points; or the needles of Becquerel (III) may be used. They consist of the same metals soldered in a straight line, one behind the other. The needles must always be covered by a varnish, which will prevent the parenchymatous juices from acting upon them, and so causing a current. Before the experiment we must determine what extent of excursion on the scale is obtained with a certain temperature. In order to determine this, a delicate thermometer is fixed to each of the thermo-couples, and both are placed in oil baths, which differ in temperature—say by 1°C .—as can be determined by the thermometer. When the current is closed, the excursion on the scale will indicate 1°C . Suppose that the excursion was 150 mm., then each mm. of the scale would be equal to $\frac{1}{150}^\circ \text{C}$. When this is determined, the two thermo-needles may be placed in the different tissues or organs of animals, and, of course, we obtain the difference of temperature in these places. Or one thermo-couple may be placed in a bath of constant temperature (nearly that of the body), in which is placed a delicate thermometer, while the other needle is introduced into the organ to be investigated. In this case we obtain the difference of temperature between the tissue and the source of the constant heat. The electric current passes in the warmer needle from the iron to the German silver, and thus through the wires of the apparatus. For small differences of temperature, such as occur in the body, the thermo-electric energy is always proportional to the difference of temperature of the two needles or couples. In place of a single pair of needles several may be used, whereby the sensitiveness of the apparatus is greatly increased. Helmholtz found that by using sixteen antimony-bismuth couples, he could detect an increase of $\frac{1}{4000}^\circ \text{C}$. Schiffer prepared a simple thermopile (IV) by soldering together alternately four pairs of wires of iron (f) and German silver (a). These are placed in the two organs (A and B) which are to be investigated, whereby a very high degree of exactness is obtained.

209. TEMPERATURE TOPOGRAPHY.—Although the blood, in virtue of its continual motion (completing, as it does, the circulation in twenty-three seconds), must exercise a very considerable influence on the equilibration of the temperature

in different organs, nevertheless, a completely uniform temperature does not exist, and the temperature varies in different parts :—

1. **Skin** (*J. Davy*).

Middle of the sole of the foot, ...	32·26° C.	Middle of upper arm, ...	35·40° C.
Near tendo Achillis, ...	33·85	Inguinal fold, ...	35·80
Anterior surface of leg, ...	33·05	Near cardiac impulse, ...	34·40
Middle of calf, ...	33·85	Face, ...	31·00
Bend of knee, ...	35·00	Nose and tip of ear, ...	22·24

In the closed axilla, 36·49 (mean, of 505 individuals) ;—36·5 to 37·25 (*Wunderlich*) ;—36·89° C. (*Liebermeister*). The skin over muscles is warmer than that over bone (*Kunkel*).

The temperature of the skin of the head is higher in the forehead and parietal region than in the occipital region ; the skin on the left side of the head is warmer than on the right. Dyspnoea increases the temperature of the skin.

Method.—*Liebermeister* determines the temperature of free cutaneous surfaces thus :—The bulb of the thermometer is heated slightly above the temperature expected ; after the mercury begins to fall, the bulb is placed on the skin, and if the bulb has the same temperature as the skin, the mercury remains stationary. This experiment must be repeated several times.

2. **Cavities.**

Mouth under the tongue, ...	37·19° C.	Vagina, ...	38·30° C.
Rectum, ...	38·01	Urine, ...	37·03

Uterine cavity somewhat warmer ; cervical canal of the uterus somewhat cooler.

The temperature falls in the **stomach** during digestion (§ 166, 1). Cold injections (11° C.) into the rectum rapidly lower the temperature in the stomach 1° C. (*Winternitz*).

3. **The temperature of the blood** is, as a mean, 39° C. The venous blood in internal viscera is warmer than the arterial, but it is cooler in peripheral parts :—

Blood of the right heart, ...	38·8°	Blood of the superior vena cava, ...	36·78°
„ left heart, ...	38·6	„ inferior vena cava, ...	38·11
„ aorta, ...	38·7	„ erural vein, ...	37·20
„ hepatic vein, ...	39·7	(Cl. Bernard and v. Liebig.)	

The lower temperature of the blood in the left heart may be explained by the blood becoming cooled in its passage through the lungs during respiration. According to Heidenhain and Körner, the right heart is slightly warmer because it lies in relation with the warm liver, whilst the left heart is surrounded by the lung, which contains air. This observation is disputed by others, who say that the left heart is slightly warmer because the combustion-processes are more active in arterial blood, and heat is evolved during the formation of oxyhæmoglobin. The blood in the veins is usually cooler than in the corresponding arteries, owing to the superficial position of the former, whereby they give off heat during their long course ; thus the blood of the jugular vein is $\frac{1}{2}$ to 2° C. lower than the blood in the carotid ; the erural vein $\frac{3}{4}$ to 1° cooler than in the erural artery. Superficial veins, more especially those of the skin, give off much heat, and their blood is, therefore, somewhat cooler. The warmest blood is that of the hepatic vein 39·7° C., partly owing to the great chemical changes which occur within the liver, from its secretory activity (§ 210, a), and partly to its protected situation.

4. The individual tissues are warmer : (1) the greater the transformation of kinetic energy into heat, i.e., the greater the tissue-metabolism ; (2) the more blood they contain ; (3) and the more protected their situation. According to Heidenhain and Körner, the cerebrum is the warmest organ of the body.

Subcutaneous tissue (sheep), ...	37·35° C.	Rectum, ...	40·67° C.
Brain, ...	40·25	Right heart, ...	41·60
Liver, ...	41·25	Left heart, ...	40·90
Lungs, ...	41·40	(Berger.)	

Bequerel and Brechet found the temperature of the human subcutaneous tissue to be 2·1° C. lower than that of the neighbouring muscles. The horny tissues do not produce heat, and their low temperature is due to the conduction of heat from the parts on which they grow. The temperature of the cornea partly depends on that of the iris, and the more contracted the pupil is, the more heat it receives from the blood-vessels of the iris.

210. CONDITIONS AFFECTING THE TEMPERATURE OF ORGANS.—The temperature of the individual organs is by no means constant ; it is influenced by many conditions ; amongst these are the following :—

(1) *The more heat produced independently within a part, the higher is its temperature.* As the amount of heat produced within a part depends upon its metabolism, therefore when the metabolism is increased, the amount of heat produced is similarly increased.

(a) **Glands** produce more heat during the act of **secretion**, as is proved by the higher temperature of their secretion, or by the higher temperature of the **venous blood** flowing out of their veins.

Ludwig found that when he stimulated the chorda tympani, the **saliva** of the submaxillary gland was 1.5° C. warmer than the blood in the carotid, which supplied the gland with blood (p. 249). The blood in the renal vein in a kidney which is secreting is warmer than the blood in the renal artery. The secreting liver produces much heat (§ 178). Cl. Bernard investigated the temperature of the blood of the portal and hepatic veins during hunger, at the beginning of digestion, and when digestion was most active, and he found:—

Temperature of portal vein, . . .	37.8° C.	} After 4 days' starvation.	} Blood of right heart, 38.8° (Hunger period.)	
„ hepatic vein, . . .	38.4			
Temperature of portal vein, . . .	39.9	} Beginning of digestion.	} Blood of right heart, during digestion, 39.2°	
„ hepatic vein, . . .	39.5			
Temperature of portal vein, . . .	39.7	} Digestion most active.		
„ hepatic vein, . . .	41.3			

In the dog a moderate diet, chemical or mechanical stimulation of the gastric mucous membrane, or even the sight of food, raises the temperature in the stomach and intestine.

(b) When the **muscles contract**, they evolve heat. Davy found that an active muscle became 0.7° C. warmer; while Becquerel, by means of a thermo-galvanometer, found that human muscles, when kept contracted for five minutes, became 1° C. warmer (§ 302).

This is one of the reasons why the temperature may rise above 40° during rapid running. A temperature obtained by energetic muscular action usually does not fall to the normal until after resting for $1\frac{1}{2}$ hour. The low temperature of paralysed limbs depends partly upon the absence of the muscular contractions.

(c) With regard to the **effect of sensory nerves** upon the temperature, some of the chief points to ascertain are—whether the *circulation* is accelerated or retarded by their stimulation, or whether the *respiration* is increased or diminished (§ 214, II., 3), and whether the *muscles of the skeleton* are relaxed or contracted reflexly (§ 214, I., 3). In the former case the temperature of the interior of the body and rectum is increased; in the latter diminished.

(d) The temperature of the body rises during **mental exertion**. Davy observed an increase of 0.3° C. after vigorous mental exertion.

(e) The parenchymatous fluids, serous fluids, and lymph produce little heat, owing to their feeble metabolism, hence they have the same temperature as their surroundings; the epidermal and horny tissues do not produce heat, they merely conduct it from subjacent structures.

(2) *The temperature depends, to a large extent, upon the amount of blood in an organ, and also upon the rapidity with which the blood is renewed by the circulation.* This is best observed in the difference of the temperature between a cold, pale, bloodless hand, and a warm, red congested one.

Becquerel and Breehet found that the temperature of the human biceps fell several tenths of a degree when the axillary artery was compressed. Ligature of the crural artery and vein in a dog causes a fall of several degrees. If the extremities be kept suspended in the air, they become bloodless and cold.

Liebermeister has pointed out a difference with regard to the external and internal parts of the body. The **external parts** give off more heat than they produce, so that they become cooler the more slowly new blood flows into them, and warmer the greater the rapidity of the blood-stream through them. Acceleration of the blood-stream, therefore, causes the temperature of peripheral parts to approximate more and more to the temperature of internal organs, while retardation of the blood-stream causes them to approach the temperature of the surrounding medium. Exactly the reverse is the case with **internal parts**, where a large amount of heat is produced, and heat is given up almost alone to the blood which flows through them. Their

temperature must fall when the blood-stream through them is accelerated, and it is raised when the blood-stream is retarded. Hence it follows that the *greater the difference of the temperature between peripheral and internal parts, the slower must be the velocity of the circulation.*

(3) If the **position** or other condition of an **organ** be such as to cause it to give off heat by **conduction** or **radiation**, then its temperature *falls*.

A good example of this is the **skin**, which varies greatly in temperature according to the temperature of the surrounding medium, whether it is covered or uncovered, whether it is dry or moist with sweat (which abstracts heat when it evaporates). When much cold food or drink is taken, the **stomach** is cooled, and when ice-cold air is breathed, the **respiratory passages** as far as the bronchi are cooled.

211. ESTIMATION OF HEAT.—Calorimetry is the method of determining the amount of heat possessed by any body, or what amount of heat it is capable of producing. The unit of measurement is the “**heat-unit**,” or “**calorie**,” *i.e.*, the amount of heat (or potential energy) required to raise the temperature of 1 gram of water 1° C. (see *Introduction*). This is sometimes called the small calorie.

Experiment has shown that *equal quantities of different substances require very unequal amounts of heat to raise them to the same temperature, e.g., 1 kilo. water requires nine times as much heat as 1 kilo. iron to raise it to the same temperature.* In the human body, therefore, which is composed of very different substances, unequal amounts of heat will be required to raise them all to the same temperature. The same amount of heat transferred to two different substances will raise them to different temperatures. Hence, bodies of different temperatures may contain equal amounts of heat. The amount of heat required to raise a definite quantity (*e.g.*, 1 grm.) of a substance to a certain higher degree (*e.g.*, 1° C.) is called “**specific heat**.” The specific heat of water (which of all bodies has the highest specific heat) is taken as = 1. By “**heat-capacity**” is meant that property of bodies in virtue of which they must absorb a given amount of heat in order to have a certain temperature.

Calorimetry is employed :—I. *To determine the specific heat of the different organs of the body.*—Only a few observations have been made. The **mean specific heat** of the following animal parts (water = 1) is :—

Human blood	= 1.02 (?)	Human muscle	= 0.741	Fat tissue	= 0.712
Arterial blood	= 1.031 (?)	Ox muscle	= 0.787	Striped muscle	= 0.825
Venous blood	= 0.892 (?)	Compact bone	= 0.3	Defibrinated blood	= 0.927
Cow's milk	= 0.992	Spongy bone	= 0.71	(J. Rosenthal.)	

The specific heat of the *human body*, as a whole, is about that of an equal volume of water.

Kopp's Method.—The *solid* to be investigated is broken in pieces about the size of a pea, and placed in a test-tube A, with thin walls, which is closed above with a cork, from which a copper wire with a hook on it projects (fig. 285). The test-tube contains a certain quantity of fluid which does not dissolve the substance, but which lies between its pieces and covers it. It is weighed three times to ascertain the weight (1) of the empty glass, (2) after it is filled with the solid substance, (3) after the fluid is added, so that we obtain the weight of the solid substance, *m*, and that of the fluid, *f*. The test-tube and its contents are placed in a *mercury bath*, BB, and this again in an *oil bath*, CC, and the whole is raised to a high temperature. Into BB there is introduced a fine thermometer, T. When the tube, A, has reached the necessary temperature (say 40°) it is rapidly placed in the water of the accompanying calorimeter-box, DD. The water in this box, which also contains a thermometer, D, is kept in motion until it has completely absorbed all the heat given off by A. Let T represent the temperature to which A and its contents were raised in

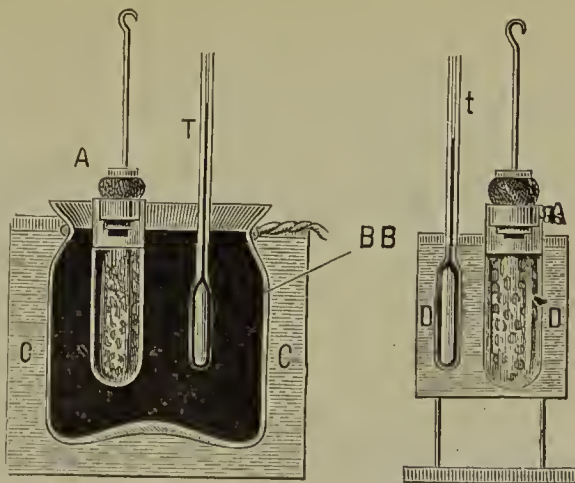


Fig. 285.

Kopp's apparatus for estimating specific heat.

the mercury bath, and T the temperature to which it fell in the calorimeter; let s be the specific heat, and m the weight of the solid substance in the test-tube, while σ and μ represent the specific heat and the weight of the interstitial fluid in the test-tube; and lastly, let w equal the amount of water in contact with A , which absorbs and gives off heat; then W represents the amount of heat which the test-tube and its contents give off during cooling.

$$W = (s \cdot m + w + \sigma \mu) (T - T_1).$$

The amount of heat, W_1 , absorbed by the calorimeter is

$$W_1 = M (t_1 - t),$$

where M represents the amount of water in the calorimeter, t the original temperature of the water in the calorimeter, and t_1 the temperature to which it is raised by placing A in it. If W and W_1 are equal, then

$$\text{the specific heat, } s = \frac{M(t_1 - t) - (w + \sigma \cdot \mu)(T - T_1)}{m(T - T_1)}.$$

If a fluid substance is placed in the test-tube, and its weight = m , and its specific heat = s , the formula for the specific heat of the fluid to be investigated is

$$s = \frac{M(t_1 - t) - w (T - T_1)}{m (T - T_1)}.$$

II. Calorimetry is more important for determining the amount of heat produced in a given time by the body as a whole, or by its *individual parts*.

Lavoisier and Laplace made the first calorimetric observations on animals in 1783, by means of an ice-calorimeter; a guinea-pig melted 13 oz. of ice in ten hours. Crawford, and afterwards Dulong and Despretz, used Rumford's water-calorimeter, which is similar to Favre and Silbermann's. Small animals are placed in the inner thin-walled copper chamber (K), which is placed in a water-bath surrounded on all sides by some non-conducting material. We require to know the amount of water, and its original temperature. The number of calories is obtained from the increase of the temperature at the end of the experiment, which lasts several hours. The air is supplied to the animal through a special apparatus, resembling a gasometer. The amount of CO_2 in the gases evolved is estimated.

According to Despretz, a bitch formed 16,410 heat-units per hour—*i.e.*, 393,000 in twenty-four hours. Other things being equal, a man seven times heavier than this would produce in twenty-four hours about 2,750,000 calories. Senator found that a dog weighing 6330 grms. produced 15,370 calories per hour, and excreted at the same time 367 grms. CO_2 . The first calorimetric experiments on man were made by Scharling (1849). Liebermeister estimated the amount of heat given off by a man placed in a cold bath, which was surrounded with a woollen covering. Leyden placed a lower limb in the calorimeter, whereby 6000 grms. water were raised 1°C . in an hour. If we assume that the total superficial area of the body is fifteen times greater than that of the leg, the human body would produce 2,376,000 calories in twenty-four hours.

212. THERMAL CONDUCTIVITY OF TISSUES.—The thermal conductivity of animal tissues is of special interest in connection with the skin and subcutaneous fatty tissue. The fatty layer under the skin, more especially in the whale, walrus, and seal, forms a protective covering, whereby the conduction of heat from internal organs is rendered almost impossible. Investigations upon this subject, however, are few. Griess attempted to estimate the thermal conductivity by heating one part of the tissue, and determining when and in what direction pieces of wax placed on the tissue to be investigated began to melt. He investigated the stomach of the sheep, the bladder, skin, hoof, horn, and bones of an ox, deer's horn, ivory, mother-of-pearl, shell of haliotis. He found that fibrous tissues conducted heat more readily in the direction of their fibres than at right angles to the course of the fibres. Hence, the figures obtained from the melted wax were usually elliptical. Landois has made similar observations, and he finds that tissues conduct better in the direction of their fibres. After bones, blood-clot was the best conductor, then followed spleen, liver, cartilage, tendon, muscle, elastic tissue, nail and hair, bloodless skin, gastric mucous membrane, washed fibrin. It is specially interesting to note how much better skin containing blood in its blood-vessels conducts than does bloodless skin. Hence little heat is given off from a bloodless skin, while congested skin conducts and gives off much more heat.

Like all other substances, the human body is enlarged by heat. A man weighing 60 kilos., and whose temperature is raised from 37°C . to 40°C ., is enlarged about 62 cubic centimetres.

Connective-tissue (tendon) is extended by heat; while elastic tissue and the skin, like caoutchouc, are contracted.

213. VARIATIONS OF THE MEAN TEMPERATURE.—(1) **General Climatic and Somatic Influences.**—In the **tropics** the mean temperature of the body is about $\frac{1}{2}^{\circ}$ C. higher than in **temperate climates**, where again it is several tenths of a degree warmer than in **cold climates**; but this has recently been denied. The difference is comparatively trivial, when we remember that a man is subjected to a variation of over 40° C. in passing from the equator to the poles. Observations on more than 4000 persons show that when a person goes from a warm to a cold climate, his temperature is but slightly diminished, but when he goes from a cold to a warm climate his temperature rises relatively considerably more. In the *temperate* zone, the temperature of the body during a *cold winter* is usually 0.1° to 0.3° C. lower than it is on a warm summer day. The **height of a place** above sea-level has no obvious effect on the temperature of the body. There seems to be no difference in different **races**, nor in the **sexes**, other conditions being the same. Persons of powerful physique and **constitution** are said to have generally a slightly higher temperature than feeble, weak, anæmic persons.

(2) **Influence of the General Metabolism.**—As the formation of heat depends upon the transformation of chemical compounds, whose chief final products, in addition to H_2O , are CO_2 and urea, the amount of heat formed must go *pari passu* with the amount of these excreta. The more rapid metabolism which sets in after a full meal causes a rise of temperature to several tenths of a degree ("Digestion-fever"). As the metabolism is much diminished during **hunger**, this explains why the mean temperature in a fasting man is 36.6° , while it is 37.17° on ordinary days (§ 237).

Jürgensen also found that the temperature fell on the first day of **inanition** (although there was a temporary rise on the second day). In experiments made upon starving animals, the temperature at first fell rapidly, then remained constant for a considerable time, while during the last days it fell considerably. Schmidt starved a cat—on the 15th day the temperature was 38.6° ; on the 16th, 38.3° ; 17th, 37.64° ; 18th, 35.8° ; 19th (death)= 33.0° . Chossat found that starving mammals and birds had a temperature 16° C. below normal on the day of their death.

(3) **Age** has a decided effect upon the temperature of the body. The extent of the general metabolism is in part an index of the heat of the body at different ages, but it is possible that other, as yet unknown, influences are also active.

Age.	Mean Temperature at the Ordinary Temperature.	Normal Limits.	Where Measured.
Newly-born,	37.45° C.	$37.35-37.55^{\circ}$ C.	Rectum.
5-9 year,	37.72	$36.87-37.62$	Mouth and Rectum.
15-20 "	37.37	$36.12-38.1$	Axilla.
21-30 "	37.22	...	"
25-30 "	36.91	...	"
31-40 "	37.1	$36.25-37.5$	"
41-50 "	36.87	...	"
51-60 "	36.83	...	"
80 "	37.46	...	Mouth.

Newly-born animals exhibit peculiarities owing to the sudden change in their conditions of existence. Immediately after birth, the infant is 0.3° warmer than the vagina of the mother, viz., 37.86° . A short time after birth the temperature falls 0.9° , while twelve to twenty-four hours afterwards it has risen to the normal temperature of an infant, which is 37.45° . Several irregular variations occur during the first weeks of life. During sleep the temperature of an infant falls 0.34° to 0.56° , while continued crying may raise it several tenths of a degree.

Old people, on account of their feeble metabolism, produce little heat; they become cold sooner, and hence ought to wear warm clothing to keep up their temperature.

(4) **Periodical Daily Variations.**—In the course of twenty-four hours there are regular periodic variations in the mean temperature, and these occur at all ages. As a general rule, the temperature *continues to rise during the day* (maximum at 5 to 8 P.M.), while it continues to *fall during the night* (minimum 2 to 6 A.M.). The mean temperature occurs at the third hour after breakfast (fig. 286).

The mean height of all the temperatures taken during a day in a patient is called the “daily mean,” and according to Jaeger it is 37.31° in the rectum in health.

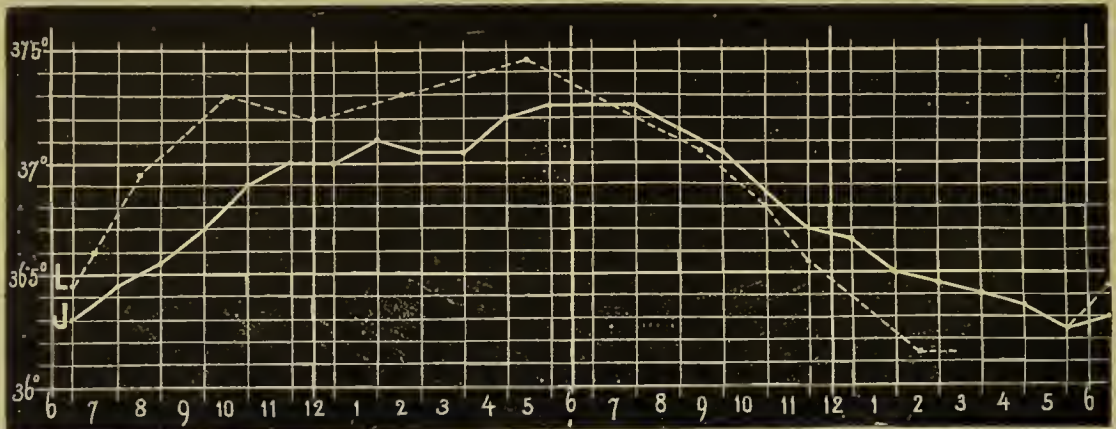


Fig. 286.

Variations of the daily temperature in health during twenty-four hours. L—, after Liebermeister; J—, after Jürgensen.

A daily mean of more than 37.8° is a “fever temperature,” while a mean under 37.0° C. is regarded as a “collapse temperature.”

Time.	Bärensprung.	J. Davy.	Hallmann.	Gierse.	Jürgensen.		Jaeger.
Morning, 5	...	...	...	...	36.7	36.6	36.9
	...	...	...	...	36.7	36.4	37.1
	6 36.68	...	...	...	36.7*	36.5*	37.5*
	7 ...	36.94*	36.63	36.98	36.8	36.7	37.4
	8 37.16*	...	36.80*	37.08*	36.9	36.8	37.5
9	...	36.89	...	...	37.0	37.0	37.5
	10 37.26	...	$10\frac{1}{2} = 37.36$	37.23	37.2	37.2	37.3
	11 ...	36.89	...	...	37.3*	37.3*	37.5*
	12 36.87	...	...	...	37.3	37.3	37.4
	1 36.83	...	37.21	37.13	37.4	37.4	37.5
Mid-day, 2	...	37.05	...	37.50*	37.4*	37.3*	37.5
	3 37.15*	...	...	37.43	37.4	37.3	37.5*
	4 ...	37.17	...	...	37.5	37.5	37.5
	5 37.48	37.05*	$5\frac{1}{2} = 37.31$	37.43	37.5	37.6	37.4
	6 ...	$6\frac{1}{2} = 36.83$	...	37.29	37.5*	37.6*	37.3
7	37.43	$7\frac{1}{2} = 36.50*$	37.31*	...	37.4	37.7	37.1*
	8 ...	...	...	...	37.4	37.5	36.9
	9 37.02*	...	...	...	37.3	37.4	36.8
	10 ...	...	...	37.29	37.2	37.1	36.8
	11 36.85	36.72	36.70	36.81	37.1	36.9	36.9
Night, 12	...	...	...	...	37.0	36.9	36.9
	1 36.65	36.44	...	...	36.9	36.7	36.8
	2 ...	...	...	...	36.8	36.7	36.7
	3 ...	...	...	...	36.7	36.7	36.7
4	36.31	...	...	...			

As the variations occur when a person is **starved** for a day—although those that occur at the periods at which food ought to have been taken are less—it is obvious that the variations are not due entirely to the taking of food. [The * indicates taking of food.]

The daily variation in the **frequency of the pulse** often coincides with variation of the temperature. Bärensprung found that the mid-day temperature maximum slightly preceded the pulse maximum (§ 70, 3, C).

If one sleeps during the day, and does all one's daily duties during the night, the above described typical course of the temperature is reversed. With regard to the effect of activity or rest, it appears that the activity of the muscles during the day tends to increase the mean temperature slightly, while at night the mean temperature is less than in the case of a person at rest.

The **peripheral parts** of the body exhibit more or less regular variations of their temperature. In the **palm** of the hand, the progress of events is the following:—after a relatively high night temperature there is a rapid fall at 6 A.M., which reaches its minimum at 9 to 10 A.M. This is followed by a slow rise, which reaches a high maximum after dinner; it falls between 1 to 3 P.M., and after two or three hours reaches a minimum. It rises from 6 to 8 P.M., and falls again towards morning. A rapid fall of the temperature in a peripheral part corresponds to a rise of temperature in internal parts.

(5) **Many operations** upon the body affect the temperature. After **hæmorrhage** the temperature falls at first, but it rises again several tenths of a degree, and is usually accompanied by a shiver or slight rigor; several days thereafter it falls to normal, and may even fall somewhat below it. The sudden loss of a large amount of blood causes a fall of the temperature of $\frac{1}{2}$ to 2° C. Very long-continued hæmorrhage (dog) causes it to fall to 31° or 29° C.

This is obviously due to the diminution of the processes of oxidation in the anæmic body, and to the enfeebled circulation. Similar conditions causing diminished metabolism effect the same result. Continued stimulation of the peripheral end of the vagus, so that the heart's action is enormously slowed, diminishes the temperature several degrees in rabbits (*Landois and Ammon*).

The **transfusion** of a considerable quantity of **blood** raises the temperature about half an hour after the operation. This gradually passes into a febrile attack, which disappears within several hours. When blood is transfused from an artery to a vein of the same animal, a similar result occurs (§ 102).

(6) **Many poisons** diminish the temperature, *e.g.*, chloroform and the anæsthetics, **alcohol** (§ 235), digitalis, **quinine**, aconitin, muscarin. These appear to act partly by rendering *the tissues less liable to undergo molecular transformations* for the production of heat. In the case of the anæsthetics, this effect perhaps occurs, and is due possibly to a semi-coagulation of the nervous substance (?). They may also act partly by influencing the **giving off of heat** (§ 214, II.). Other poisons increase the temperature for opposite reasons.

The temperature is increased by **strychnin**, nicotin, pierotoxin, veratrin, landanin.

(7) Various **diseases** diminish the temperature, which may be due either to lessened production of heat (diminution of the metabolism), or to increased expenditure of heat. Loewenhardt found that in paralytics and in insane persons, several weeks before their death, the rectal temperature was 30° to 31° C., in diabetes 30° C. or less; the lowest temperature observed and life retained in a drunk person was 24° C.

The temperature is increased in *fever*, and the highest point reached just before death, and recorded by Wunderlich, was 44.65° C. (compare § 220).

214. REGULATION OF THE TEMPERATURE.—As the bodily temperature of man and similar animals is **nearly constant**, notwithstanding great variations in the temperature of their surroundings, it is clear that some mechanism must exist in the body, whereby the heat economy is **constantly regulated**. This may be brought about in **two ways**; either by controlling the transformation of potential energy into heat, or by affecting the amount of heat given off according to the amount produced, or to the action of external agencies.

[The constancy or thermostatic condition of the temperature is brought about by

three co-operant factors, the **thermogenic** or heat-producing, the **thermolytic** or heat-discharging, and the **thermotaxic** or mechanism by which heat-production and heat-loss are balanced, and it is obvious that the last must be in relation with the other two. The thermotaxic mechanism is developed last, is least pronounced in the lower vertebrata, and is most *easily* liable to fail under injury or disease (*MacAlister*).]

I. Regulatory Arrangements governing the Production of Heat.—Liebermeister estimated the amount of heat produced by a healthy man at 1·8 calories, *i.e.*, the kilo unit, per minute. It is highly probable that, within the body, there exist mechanisms which determine the molecular transformations, upon which the evolution of heat depends. This is accomplished chiefly in a **reflex manner**. The peripheral ends of cutaneous nerves (by thermal stimulation), or the nerves of the intestine and the digestive glands (by mechanical or chemical stimulation during digestion or inanition), may be irritated, whereby impressions are conveyed to the **heat-centre**, which sends out impulses through efferent fibres to the depôts of potential energy, either to increase or diminish the extent of the transformations occurring in them. The nerve-channels herein concerned are entirely unknown. Many considerations, however, go to support such an hypothesis (§ 377).

[**Thermotaxic Mechanism, Thermal Nerves and Centres.**—Just as the respiration and the state of the blood-vessels are regulated from a central focus, so the question arises, Does the same obtain with regard to temperatures? Studying this question, however, it must be borne in mind that thermometric observations alone are not sufficient; the true test must be calorimetric. Sir Benjamin Brodie observed that in a case of injury of the spinal cord in the neck the temperature in the thigh rose very high. In some cases the temperature falls. Wood has shown that section of the cord above the origin of the splanchnics leads to decided increase in the amount of heat dissipated, but to a decided diminution of heat-production. The vaso-motor paralysis has much to do in these cases with the loss of heat. In warm-blooded animals, exposed to a high temperature, the heat-production is diminished, but when they are exposed to a low temperature it is increased. If a warm-blooded animal's medulla oblongata be divided, there is a fall of temperature, chiefly due to vaso-motor paralysis, and such an animal behaves, as regards the effect of heat and cold, exactly like a poikilothermal animal, *i.e.*, its metabolism and heat-production are increased by cold and diminished by heat. If, however, the incision be made above the pons, so as to leave the vaso-motor centre intact in the dog, there is a rise of the temperature and increased heat-production for 24 hours afterwards. This suggests the idea that this region is traversed by inhibitory nerves, so that when they are cut off from their centres situate above, the augmentor nerves can act more vigorously. This suggests the existence of thermo-inhibitory centres situate higher up in the brain. If an animal be curarised, not only is there paralysis of voluntary motor acts, but on stimulating an ordinary motor nerve, not only is there no muscular contraction, but there is no rise of temperature of the muscles supplied by that nerve. In such an animal the temperature rises and falls with the temperature of the surrounding medium. Even although the respirations be kept constant and the vaso-motor nerves intact, the thermogenic activity of muscles, therefore, seems to be dependent on their innervation.]

[**Cerebral Centres.**—Apart from the cortical heat centres (§ 377), Ott, Aronsohn, Sachs, Richet, and others have shown that if a needle be thrust through the skull and brain, so as to injure certain deeper-seated parts, there is a rise of temperature and increased heat-production for several hours. The experiment may be repeated several times in the same rabbit. Ott gives three areas which, when so injured, cause these effects—(1) a part of the brain in the median side of the corpus striatum, and near the nodus cursorius; (2) a part between the corpus striatum and the optic thalamus; and (3) the anterior end of the optic thalamus itself. From the effect of atropin, Ott suggests the existence of spinal centres as well.]

Regulatory Mechanisms.—The following phenomena indicate the existence of mechanisms regulating the production of heat:—

(1) The temporary application of **moderate cold raises the bodily temperature**, while heat, similarly applied to the external surface, lowers it (§§ 222 and 224).

(2) **Cooling of the surroundings** increases the amount of CO₂ excreted, by increasing the production of heat, while the O consumed is also increased simultaneously; heating the surrounding medium diminishes the CO₂ (§ 126, 5).

D. Finkler found, from experiments upon guinea-pigs, that the production of heat was more

than doubled when the surrounding temperature was diminished 24° C. The metabolism of the guinea-pig is increased in winter 23 per cent. as compared with summer, so that the same relation obtains as in the case of the diminution of the surrounding temperature of short duration.

C. Ludwig and Sanders-Ezn found that in a rabbit there was a rapid increase in the amount of CO_2 given off, when the surroundings were cooled from 38° to 6° or 7° C.; while the excretion was diminished when the surrounding temperature was raised from 4° – 9° to 35° – 37° , so that the thermal stimulation, due to the temperature of the surrounding medium, acted upon the combustion within the body. Pflüger found that a rabbit which was dipped in cold water used more O and excreted more CO_2 .

If the cooling action was so great as to reduce the *bodily* temperature to 30° , the exchange of gases diminished, and where the temperature fell to 20° , the exchange of gases was diminished one-half. It is to be remembered, however, that the *excretion of* CO_2 does not go hand in hand with the formation of CO_2 . If mammals be placed in a *warm* bath, which is 2° to 3° higher than their own temperature, the excretion of CO_2 and the consumption of O are increased owing to the stimulation of their metabolism, while the excretion of urea is also increased in animals and in man (§ 126, 5).

(3) **Cold** acting upon the skin causes **involuntary muscular movements** (shivering, rigors), and also **voluntary movements**, both of which produce heat.

The cold excites the action of the muscles, which is connected with processes of oxidation (*Pflüger*). After poisoning with **curare**, which paralyses voluntary motion, this regulation of the heat falls to a minimum (*Rohrig and Zuntz*), [so that the bodily temperature rises and falls with a rise or fall in the temperature of the surrounding medium].

(4) Variations in the **temperature of the surroundings** affect the **appetite for food**; in winter, and in cold regions, the sensation of hunger and the appetite for the fats, or such substances as yield much heat when they are oxidised, are increased; in summer, and in hot climates, they are diminished. Thus the mean temperature of the surroundings, to a certain extent, determines the amount of the heat-producing substances to be taken in the food.

II. Regulatory Mechanisms governing the Excretion of Heat or Thermolysis.

—The mean amount of heat given off by the human skin in twenty-four hours, by a man weighing 82 kilos, is 2092 to 2952 calories, *i.e.*, 1.36 to 1.60 per minute.

[**Radiation from the Skin.**—The real radiating surface in man under ordinary conditions is the surface of the clothes, and only to a comparatively small extent the skin. In warm-blooded animals it is not the naked epidermis but the surface of the hair or feathers. The amount of radiation from this surface depends (1) on the difference between its temperature and that of the surroundings, and (2) on its co-efficient of emission. G. N. Stewart has compared the influence of these two factors for the human skin by measuring simultaneously the temperature of the skin and the amount of heat radiated from it. Both measurements were made by the electrical method with lead paper gratings. The co-efficient of emission was not found to vary much under the conditions of the experiments, the chief factor in determining the amount of radiation being the temperature difference. Masje, however, has stated that when a large part of the body is stripped in a cold atmosphere the radiation from the skin is increased, although its temperature is lowered. The effect of replacing the normal radiating surface by one of higher temperature is well seen when the hair is extensively removed from a rabbit or a guinea-pig, and the animal is prevented from covering itself. Even in warm summer weather the animal may die in as short a time as twenty hours (*G. N. Stewart*).]

(1) **Heat** causes **dilatation of the cutaneous vessels**; the skin becomes red, congested, and soft; it contains more fluids, and becomes a better conductor of heat; the epithelium is moistened, and **sweat** appears upon the surface. Thus increased excretion of heat is provided for, while the evaporation of the sweat also abstracts heat.

The amount of heat necessary to convert into vapour 1 gm. of water at 100° C. is equal to that required to heat 10 grms. from 0° to 53.67° C. The sweat as secreted is at the temperature of the body; if it were completely changed into vapour, it would require the heat necessary to raise it to the boiling point, and also that necessary to convert it into vapour.

Cold causes **contraction of the cutaneous vessels**; the skin becomes pale, less soft, poorer in juices, and collapsed; the epithelium becomes dry, and does not permit fluids to pass through it to be evaporated, so that the excretion of heat is diminished. The *excretion of heat* from the periphery, and the transverse *thermal*

conduction through the skin, are diminished by the contraction of the vessels and muscles of the skin, and by the expulsion of the well-conducting blood from the cutaneous and subcutaneous vessels. The cooling of the body is very much affected, owing to the diminution of the cutaneous blood-stream, just as occurs when the current through a coil or worm of a distillation apparatus is greatly diminished. If the blood-vessels dilate, the temperature of the surface of the body rises, the difference of temperature between it and the surrounding cooler medium is increased, and thus the excretion of heat is increased. Tomsa has shown that the fibres of the skin are so arranged anatomically, that the tension of the fibres produced by the erector pili muscles causes a diminution in the thickness of the skin, this result being brought about at the expense of the easily expelled blood.

By the systematic application of stimuli, *e.g.*, cold baths, and washing with cold water, the muscles of the skin and its blood-vessels may be caused to contract, and become so vigorous and excitable that when cold is suddenly applied to the body, or to a part of it, the excretion of heat is energetically prevented, so that cold baths and washing with cold water are, to a certain extent, "gymnastics of the cutaneous muscles," which, under the above circumstances, protect the body from cold.

(2) **Increased temperature causes increased heart-beats**, while **diminished temperature diminishes** the number of contractions of the heart (§ 58, II., *a*). The relatively warm blood is pumped by the action of the heart from the internal organs of the body to the surface of the skin, where it readily gives off heat. The more frequently the same volume of blood passes through the skin—twenty-seven heart-beats being necessary for the complete circuit of the blood—the greater will be the amount of heat given off, and conversely. Hence, the frequency of the heart-beat is in direct relation to the rapidity of cooling. In very hot air (over 100° C.) the pulse rises to over 160 per minute. The same is true in fever (§ 70, 3, *c*). Liebermeister gives the following numbers in an adult:—

Pulse-beats, per min.,	78·6	91·2	99·8	108·5	110	137·5
Temperature in C.,	37°	38°	39°	40°	41°	42°

(3) **Increased Temperature increases the Number of Respirations.**—Under ordinary circumstances, a much larger volume of air passes through the lungs when it is warmed almost to the temperature of the body. Further, a certain amount of watery vapour is given off with each expiration, which must be evaporated, thus abstracting heat. Energetic respiration aids the circulation, so that respiration acts indirectly in the same way as (2). According to other observers, the increased consumption of O favours the combustion in the body, whereby the increased respiration must act in producing an amount of heat greater than normal (§ 126, 8). This excess is more than compensated for by the cooling factors above mentioned. Forced respiration produces cooling, even when the air breathed is heated to 54° C., and saturated with watery vapour.

(4) **Covering of the body.**—Animals become clothed in winter with a winter fur or covering, while in summer their covering is lighter, so that the excretion of heat in surroundings of different temperatures is thereby rendered more constant.

Many animals which live in very cold air or water (whale) are protected from too rapid excretion of heat by a *thick layer of fat* under the skin. Man provides for a similar result by adopting summer and winter clothing.

(5) The **position of the body** is also important; pulling the parts of the body together, approximation of the head and limbs, keep in the heat; spreading out the limbs, erection of the hairs, pluming the feathers, allow more heat to be evolved. If a rabbit be kept exposed to the air with its legs extended for three hours, the rectal temperature will fall from 39° C. to 37° C. Man may influence his temperature by remaining in a warm or a cold room—by taking hot or cold drinks, hot or cold baths—remaining in air at rest or air in motion, *e.g.*, by using a fan.

CLOTHING.—Warm Clothing is the Equivalent of Food.—As clothes are intended to keep in the heat of the body, and heat is produced by the combustion and oxidation of the food, we may say the body takes in heat directly in the food, while clothing prevents it from giving off too much heat. Summer clothes weigh 3 to 4 kilos., and winter ones 6 to 7 kilos.

In connection with clothes, the following considerations are of importance:—

(1) *Their capacity for conduction.*—Those substances which conduct heat badly keep us warmest. Hare-skin, down, beaver-skin, raw silk, taffeta, sheep's wool, cotton wool, flax, spun-silk, are given in order, from the worst to the best conductors. (2) *The capacity for radiation.*—Coarse materials radiate more heat than smooth, but colour has no effect. (3) *Relation to the sun's rays.*—Dark materials absorb more heat than light-coloured ones. (4) *Their hygroscopic properties* are important, whether they can absorb much moisture from the skin and gradually give it off by evaporation, or the reverse. The same weight of wool takes up twice as much as linen; hence the latter gives it off in evaporation more rapidly. Flannel next the skin is not so easily moistened, nor does it so rapidly become cold by evaporation; hence it protects against the action of cold. (5) *The permeability for air* is of importance, but does not stand in relation with the heat-conducting capacity. The following substances are arranged in order from the most to the least permeable—flannel, buck-skin, linen, silk, leather, waxcloth.

215. HEAT-BALANCE.—As the temperature of the body is maintained within narrow limits, the amount of heat taken in must balance the heat given off, *i.e.*, exactly the same amount of potential energy must be transformed in a given time into heat, as heat is given off from the body. An adult produces as much heat in half an hour as will raise the temperature of his body 1°C . If no heat were given off, the body would become very hot in a short time; it would reach the boiling point in thirty-six hours, supposing the production of heat continued uninterruptedly. The following are the most important calculations on the subject:—

A. Helmholtz was the first to estimate numerically the amount of heat produced by a man:—

- (1) **Heat-income.**—(a) A healthy adult, weighing 82 kilos., expires in twenty-four hours 878.4 grms. CO_2 (*Scharling*). The combustion of the C therein into CO_2 produces 1,730,760 cal.
 (b) But he takes in more O than reappears in the CO_2 ; the excess is used in oxidation-processes, *e.g.*, for the formation of H_2O , by union with H, so that 13.615 grms. H will be oxidised by the excess of O, which gives 318,600 „
 2,049,360 cal.
 (c) About 25 per cent. of the heat must be referred to sources other than combustion (*Dulong*), so that the total = 2,732,000 „

2,732,000 calories are actually sufficient to raise the temperature of an adult, weighing 80 to 90 kilos., from 10° to 35° or 39°C , *i.e.*, to a normal temperature.

- (2) **Heat-expenditure.**—(a) Heating the food and drink, which have a mean temperature of 12°C 70,157 cal. = 2.6 per cent.
 (b) Heating the air respired = 16,400 grms. with an initial temperature of 20°C 70,032 „ = 2.6 „
 (*When the temperature of the air is 0° , 140,064 cal. = 5.2 per cent.*)
 (c) Evaporation of 656 grms. water by the lungs, ... 397,536 „ = 14.7 „
 (d) The remainder given off by radiation and evaporation of water by the skin, ... (77.5 per cent. to) = 80.1 „

B. Dulong.—(1) **Heat-income.**—Dulong and others sought to estimate the amount of heat from the C and H contained in the food. As we know that the combustion of 1 grm. C = 8040 heat-units, and 1 grm. H = 34,460 heat-units, it would be easy to determine the amount of heat were the C simply converted into CO_2 and the H into H_2O . But Dulong omitted the H in the carbohydrates (*e.g.*, grape-sugar = $\text{C}_6\text{H}_{12}\text{O}_6$) as producing heat, because the H is already combined with O, or at least is present in the proportion in which it exists in water. This assumption is hypothetical, for the atoms of C in a carbohydrate may be so firmly united to the other atoms, that before oxidation can take place their relations must be altered, so that potential energy is used up, *i.e.*, heat must be rendered latent; so that these considerations rendered the following example of Dulong's method given by Vierordt very problematical:—

An adult eats in twenty-four hours 120 grms. proteids, 90 grms. fat, and 340 grms. starch (carbohydrates). These contain:—

Proteids,	.	.	.	120 grms. contain	64.18 C. and	8.60 H.
Fat,	.	.	.	90 „ „	70.20 „	10.26
Starch,	.	.	.	340 „ „	146.82	...

The urine and feces contain still unconsumed, . . . 281.20 and 18.86
 29.8 „ 6.3

Remainder to be burned, . . . 251.4 and 12.56

As 1 grm. C=8040 heat-units and 1 grm. H=34,460 heat-units, we have the following calculation :—

$$251.4 \times 8,040 = 2,031,812 \text{ (from combustion of C).}$$

$$12.56 \times 34,460 = 432,818 \text{ („ „ H).}$$

2,464,130 heat-units.

(2) **Heat-Expenditure :—**

	Heat-units.	Per cent. of the excreta.
1. 1900 grms. are excreted daily by the urine and feces, and they are 25° warmer than the food, . . .	47,500	1.9
2. 13,000 grms. air are heated (from 12° to 37° C.) (heat-capacity of the air=0.26), . . .	84,500	3.38
3. 330 grms. water are evaporated by the respiration (1 grm.=582 heat-units), . . .	192,060	7.68
4. 660 grms. water are evaporated from the skin, . . .	384,120	15.37
Total, . . .	708,180	
Remainder radiated and conducted from the skin, . . .	1,791,820	71.67
Total amount of heat-units given off, . . .	2,500,000	100.00

C. Heat-income.—Frankland burned the food directly in a calorimeter, and found that 1 grm. of the following substances yielded :—

Albumin, 1 grm., . . .	4998 heat-units.
Grape-sugar, 1 grm., . . .	3217 „
Ox fat, 1 grm., . . .	9069 „

The albumin, however, is only oxidised to the stage of urea, hence the heat-units of urea must be deducted from 4998, which gives 4263 heat-units obtainable from 1 grm. albumin. When we know the number of grams consumed, a simple multiplication gives the number of heat-units.

The heat-units will vary, of course, with the nature of the food. J. Ranke gives the following :—

With animal diet, . . .	2,779,524 heat-units.
„ food free from N, . . .	2,059,506 „
„ mixed diet, . . .	2,200,000 „
„ during hunger, . . .	2,012,816 „

216. VARIATIONS IN HEAT-PRODUCTION.—(1) **Influence of Bodily Surface.**—Rubner found that the production of heat depended more upon the size of the body and its superficial area than upon the body-weight. Small or young animals have a relatively larger surface than large or older ones, and as the removal of heat takes place chiefly from the external surface, animals with a larger surface must produce more heat. Small animals use relatively more O. Rubner's investigations on dogs of different size gave a heat-production of 1,143,000 calories for every square metre of cutaneous surface. On comparing the body-weight with the cutaneous surface in different animals, he found that for every 1 kilo. of body-weight there was in the rat 1650, rabbit 946, man 287 square centimetres of surface.

(2) **Age and Sex.**—The heat-production is less in infancy and in old age, and it is less in proportion in the female than in the male.

(3) **Daily Variation.**—The heat-production shows variations in twenty-four hours corresponding with the temperature of the body (§ 213, 4).

(4) The heat-production is greater in the **waking** condition, during physical and mental exertion, and during digestion, than in the opposite conditions.

217. RELATION OF HEAT-PRODUCTION TO WORK.—The potential energy supplied to the body may be transformed into **heat** and various other forms of **kinetic energy** (see *Introduction*). In the resting condition, almost all the potential energy is changed into heat; the workman, however, transforms

potential energy into **work**—mechanical work—in addition to heat. These two may be compared by using an equivalent measurement, thus, 1 **heat-unit** (energy required to raise 1 gram of water 1° C.) = 425.5 grammetres.

Relation of Heat to Work.—The following example may serve to illustrate the relation between heat-production and the production of work:—Suppose a small steam-engine to be placed within a capacious calorimeter, and a certain quantity of coal to be burned, then as long as the engine does not perform any mechanical work, heat alone is produced by the burning of the coal. Let this amount of heat be estimated, and a second experiment made by burning the same amount of coal, but allow the engine to do a certain amount of work—say, raise a weight—by a suitable arrangement. This work must, of course, be accomplished by the potential energy of the heating material. At the end of this experiment, the temperature of the water will be much less than in the first experiment, *i.e.*, fewer heat-units have been transferred to the calorimeter when the engine was heated than when it did no work. Comparative experiments of this nature have shown that in the second experiment the useful work is very nearly proportional to the decrease of the heat (*Hirn*).

Compare this with what happens within the body:—A man in a **passive condition** forms from the potential energy of the food between $2\frac{1}{2}$ to $2\frac{3}{4}$ million calories. The **work done** by a workman is reckoned at 30,000 kilogrammetres (§ 300).

If the organism were precisely similar to a machine, a smaller amount of heat, corresponding to the work done, would be formed in the body. As a matter of fact, the organism produces less heat from the same amount of potential energy when mechanical work is done. There is one point of difference between a workman and a working machine. The workman consumes much more potential energy in the same time than a passive person; much more is transformed in his body; and hence the increased consumption is not only covered, but even over-compensated. Hence, the workman is warmer than the passive person, owing to the increased muscular activity (§ 210, 1, *b*). Take an example:—*Hirn* remained *passive*, and absorbed 30 grms. O per hour in a calorimeter, and produced 155 calories. When in the calorimeter he did work equal to 27,450 kilogrammetres, which was transferred beyond it; he absorbed 132 grms. O, and produced only 251 calories.

In estimating the work done, we must include only the heat-equivalent of the work transferred beyond the body; lifting weights, pushing anything, throwing a weight, and lifting the body, are examples. In ordinary walking we must take into account that we overcome the resistance of the air and activity of the muscles.

The organism is superior to a machine in as far as it can, from the same amount of potential energy, produce more work in proportion to heat. Whilst the very best steam-engine gives $\frac{1}{8}$ of the potential energy in the form of work, and $\frac{7}{8}$ as heat, the body produces $\frac{1}{5}$ as work and $\frac{4}{5}$ as heat. *Chemical energy* can never do work alone, in a living or dead motor, without heat being formed at the same time.

218. ACCOMMODATION FOR VARYING TEMPERATURES.—All substances which possess high conductivity for heat, when brought into contact with the skin, appear to be very much colder or hotter than bad conductors of heat. The reason of this is that these bodies abstract far more heat, or conduct more heat than other bodies. Thus the water of a cool bath, being a better conductor of heat, is always thought to be colder than air at the same temperature. In our climate it appears to us that—

Air, at 18° C. is moderately warm ;
 „ at 25° – 28° C., hot ;
 „ above 28° , very hot.

Water, at 18° C. is cold ;
 „ from 18° – 29° C., cool ;
 „ „ 29° – 35° C., warm ;
 „ „ 37.5° and above, hot.

Warm Media.—As long as the temperature of the body is higher than that of the surrounding medium, heat is given off, and that the more rapidly the better

the conducting power of the surrounding medium. As soon as the temperature of the surrounding medium rises higher than the temperature of the body, the latter absorbs heat, and it does so the more rapidly the better the conducting power of the medium. Hence hot water appears to be warmer than air at the same temperature. A person may remain eight minutes in a **bath** at 45.5° C. (dangerous to life!); the hands may be plunged into water at 50.5° C, but not at 51.65° , while at 60° violent pain is produced.

A person may remain for eight minutes in **hot air** at 127° C., and a temperature of 132° C. has been borne for ten minutes, and yet the body temperature rises only to 38.6° or 38.9° . This depends upon the air being a bad conductor, and thus it gives less heat to the body than water would do. Further, and what is more important, the skin becomes covered with sweat, which evaporates and abstracts heat, while the lungs also give off more watery vapour. The enormously increased heart-beats—over 160—and the *dilated blood-vessels*, enable the skin to obtain an ample supply of blood for the formation and evaporation of sweat. In proportion as the secretion of sweat diminishes, the body becomes unable to endure a hot atmosphere; hence it is that in *air containing much watery vapour* a person cannot endure nearly so high a temperature as in dry air, so that heat must accumulate in the body. In a Turkish vapour-bath of 53° to 60° C., the rectal temperature rises to 40.7° or 41.6° C. A person may work continuously in air at 31° C. which is almost saturated with moisture.

If a person be placed in **water** at the temperature of the body, the normal temperature rises 1° C. in one hour, and in $1\frac{1}{2}$ hour about 2° C. A gradual increase of the temperature from 38.6° to 40.2° C. causes the axillary temperature to rise to 39.0° within fifteen minutes.

219. STORAGE OF HEAT.—As the uniform temperature of the body, under normal circumstances, is due to the reciprocal relation between the amount of heat produced and the amount given off, it is clear that heat must be stored up in the body when the evolution of heat is diminished. The **skin is the chief organ regulating the evolution of heat**; when it and its blood-vessels contract, the heat evolved is diminished; when they dilate, it is increased. **Heat may be stored up** when—

(a) The *skin* is extensively *stimulated*, whereby the cutaneous vessels are temporarily contracted. (b) Any other circumstances preventing heat from being given off by the skin. (c) When the *vaso-motor centre* is *excited*, causing all the blood-vessels of the body—those of the skin included—to contract. This seems to be the cause of the rise of temperature after transfusion of blood, and the rise of temperature after the *sudden removal of water* from the body seems to admit of a similar explanation, as the inspissated blood occupies less space, and the contracted vessels of the skin admit less blood. (d) When the circulation in the cutaneous vessels of a large area is mechanically slowed, or when the smaller vessels are plugged by the injection of some sticky substance, or by the transfusion of foreign blood, the temperature rises (§ 102).

It is also obvious that when a normal amount of heat is given off, an increased production of heat must raise the temperature. The rise of the temperature after muscular or mental exertion, and during digestion, seems to be caused in this way. The rise which occurs several hours after a cold bath is probably due to the reflex excitement of the skin causing an increased production (*Jürgensen*).

When the temperature of the body, as a whole, is raised 6° C., death takes place, as in sunstroke. It seems as if there was a molecular decomposition of the tissues at this temperature; while, if a slightly lower temperature be kept up *continuously*, fatty degeneration of many tissues occurs (*Litten*). If animals, which have been exposed artificially to a temperature of over 42° to 44° C., be transferred to a cooler atmosphere, their temperature becomes sub-normal (36° C.), and may remain so for several days.

220. FEVER.—Fever consists in a “*disorder of the body heat*,” and at the same time there is greatly *increased tissue metabolism* (especially in the muscles). Of course the mechanism regulating the balance of formation and expenditure of heat is disturbed. During fever the body is greatly incapacitated for performing mechanical work. It is evident, therefore, that the large amount of potential energy transformed is almost all converted into heat, so that the non-transformation of the energy into mechanical work is another important factor. We may take intermittent fever or *ague* as a type of fever, in which violent attacks of fever of several hours’ duration alternate with periods free from fever. This enables us to analyse the symptoms. The symptoms of fever are:—

(1) The **increased bodily temperature** (38° to 39° C., slight; from 39° to 41° C. and upwards, severe).—The high temperature occurs not only in cases where the skin is red, and has a hot burning feeling (calor mordax), but even during the rigor or the shivering stage, the temperature is raised. The congested red skin is a good conductor of heat, while the pale bloodless skin conducts badly; hence, the former feels hot to the touch (§ 212).

[The following table in $^{\circ}$ C. and $^{\circ}$ F. indicates generally the degree of fever:—

35° C. = 95° F.	Collapse.	39° C. = 102.2° F. }	Moderate Fever.
36 = 96.8	Low.	39.5 = 103.1 }	
36.5 = 97.7	Sub-normal.	40 = 104 }	High fever.
37 = 98.6	Normal.	40.5 = 104.9 }	
37.5 = 99.4)	Sub-febrile.	41 = 105.8 }	Hyperpyretic.
38 = 100.4 }			
38.5 = 101.3 }			

Finlayson.]

(2) The **increased production of heat** is proved by calorimetric observations. This is, in small part, due to the increased activity of the circulation being changed into heat (§ 206, 2, a), but for the most part it is due to increased combustion within the body.

(3) The **increased metabolism** gives rise to the “*consuming*” or “*wasting*” character of fever, which was known to Hippocrates and Galen. In 1852 v. Bärensprung asserted that “all the so-called febrile symptoms show that the metabolism is increased.” The increase of the metabolism is shown in the increased *excretion of* CO_2 = 70 to 80 per cent., while more O is consumed, although the respiratory quotient remains the same. According to D. Finkler, the CO_2 excreted shows greater variations than the O consumed. The *excretion of urea* is increased $\frac{1}{3}$ to $\frac{2}{3}$. In dogs suffering from septic fever, Naunyn observed that the urea began to increase before the temperature rose, “*prefebrile rise*.” Part of the urea, however, is sometimes retained during the fever, and appears after the fever is over, “*epicritical excretion of urea*.” The *uric acid* is also increased; the *urine pigment* (§ 19), derived from the hæmoglobin, may be increased twenty times, while the excretion of *potash* may be seven-fold. It is important to observe that the oxidation or combustion processes within the body of the fever-patient are greatly increased when he is placed in a *warmer* atmosphere. The oxidation processes in fever, however, are also increased under the influence of *cooler* surroundings (§ 214, I., 2), but the increase of the oxidation in a warm medium is very much greater than in the cold (D. Finkler). The amount of CO_2 in the blood is diminished, but not at once after the onset even of a very severe fever (Geppert).

(4) The **diminished excretion of heat** varies in different stages of a fever. We distinguish several stages in a fever—(a) The **cold stage**, when the loss of heat is greatly diminished owing to the pale bloodless skin, but at the same time the heat-production is increased $1\frac{1}{2}$ to $2\frac{1}{2}$ times. The sudden and considerable rise of the temperature during this stage shows that the diminished excretion of heat is not the only cause of the rise of the temperature. (b) During the **hot stage** the *heat given off* from the congested red skin is *greatly increased*, but at the same time more heat is produced. Liebermeister assumes that a rise of 1, 2, 3, 4° C. corresponds to an increased production of heat of 6, 12, 18, 24 per cent. (c) In the **sweating stage** the excretion of heat through the red moist skin and evaporation are greatest, more than two or three times the normal. The heat-production is either increased, normal, or sub-normal, so that under these conditions the temperature may also be sub-normal (36° C.).

(5) The **heat-regulating mechanism is injured**.—A warm temperature of the surroundings raises the temperature of the fever-patient more than it does that of a non-febrile person. The depression of the heat-production, which enables normal animals to maintain their normal temperature in a warm medium (§ 214), is much less in fever (D. Finkler).

The **accessory phenomena** of fever are very important:—Increase in the intensity and number of the heart-beats (§ 214, II., 2) and respirations (in adults 40, and children 60 per min.) both being compensatory phenomena of the increased temperature; further, diminished digestive activity and intestinal movements (§ 186, D); disturbances of the cerebral activities; of secretion; of muscular activity; slower excretion, *e.g.*, of potassium iodide through the urine. In severe fever, molecular degenerations of the tissues are very common. For the condition of the blood-corpuscles in fever, see § 10, the vascular tension, § 69, the saliva, § 146, digestion, § 186.

Quinine, the most important febrifuge, causes a decrease of the temperature by limiting the

production of heat (§ 213, 6). Toxic doses of the metallic salts act in the same way, while there is at the same time diminished formation of CO_2 [**Antipyretics or Febrifuges**.—All methods which diminish abnormal temperature belong to this group. As the constant temperature of the body depends on (1) the amount of heat-production, and (2) the loss of heat, we may lower the temperature either in the one way or the other. When cold water is applied to the body, it abstracts heat, *i.e.*, it affects the results of fever, so that Liebermeister calls such methods **antithermic**. But those remedies which diminish the actual heat-production are true **antipyretics**. In practice, however, both methods are usually employed, and spoken of collectively as antipyretic.]

[Amongst the methods which are used to abstract heat from the body are the application of colder fluids, such as the cold bath, diffusion, douche, spray, ice, or cold mixtures, &c. A person suffering from high fever requires to be repeatedly placed in a cold bath to produce any permanent reduction of the temperature. Some remedies act by favouring the radiation of heat, by dilating the cutaneous vessels (alcohol), while others excite the sweat-glands—*i.e.*, are **sudorifics**—so that the water by its evaporation removes some heat. Amongst the drugs which influence tissue changes and oxidation, and thereby lessen heat-production, are quinine, salicylic acid, some of the salicylates, digitalis, and veratrin. Blood-letting was formerly used to diminish abnormal temperature. Amongst the newer antipyretic remedies are hydrochlorate of kairin and antipyrin, both of which belong to the aromatic group (derivatives of benzol), which includes also many of our best antiseptics.]

221. ARTIFICIAL INCREASE OF THE BODILY TEMPERATURE.—If mammals are kept *constantly* in air at 40°C ., the excretion of heat from the body ceases, so that the heat produced is stored up. At first the temperature falls somewhat for a very short time, but soon a decided increase occurs. The respirations and pulse are increased, while the latter becomes irregular and weaker. The O absorbed and CO_2 given off are diminished after six to eight hours, and death occurs when the bodily temperature has been increased 4° or at most 6°C . Death does not take place owing to rigidity of the muscles, for the coagulation of the myosin of mammals' muscles occurs at 49° to 50°C ., in birds at 53°C ., and in frogs at 40°C . If mammals are *suddenly* placed in air at 100°C ., death occurs (in 15 to 20 min.) very rapidly, and with the same phenomena, while the bodily temperature rises 4° to 5°C . In rabbits the body-weight diminishes 1 gm. per min. Birds bear a high temperature somewhat longer; they die when their blood reaches 48° to 50°C .

Even **man** may remain for some time in air at 100 – 110 – 132°C ., but in ten to fifteen minutes there is danger to life. The skin is burning to the touch, and red; a copious secretion of sweat bursts forth, and the cutaneous veins are fuller and redder. The pulse and respirations are greatly accelerated. Violent headache, vertigo, feebleness, and stupefaction, indicate great danger to life. The rectal temperature is only 1° to 2°C . higher. The high temperature of fever may even be dangerous to human life. If the temperature remains for any length of time at 42.5°C ., death is almost certain to occur. Coagulation of the blood in the arteries is said to occur at 42.6°C . If the artificial heating *does not produce death*, fatty infiltration and degeneration of the liver, heart, kidneys, and muscles begin after thirty-six to forty-eight hours.

Cold-blooded animals, if placed in hot air or warm water, soon have their temperature raised 6 to 10°C . The highest temperature compatible with life in a frog must be below 40°C ., as the frog's heart and muscles begin to coagulate at this temperature. Death is preceded by a stage resembling death, during which life may be saved.

Most of the **juicy plants** die in half an hour in air at 52°C ., or in water at 46°C . (*Sachs*). Dried seeds of corn may still germinate after long exposure to air at 120°C . Lowly organised plants, such as algae, may live in water at 60°C . (*Hoppe-Seyler*). Several bacteria withstand a boiling temperature (*Tyndall*).

222. EMPLOYMENT OF HEAT.—**Action of Heat.**—The short, but not intense, action of heat on the surface causes, in the first place, a transient slight decrease of the bodily temperature, partly because it retards reflexly the production of heat, and partly because, owing to the dilatation of the cutaneous vessels and the stretching of the skin, more heat is given off. A warm bath above the temperature of the blood at once increases the bodily temperature.

Therapeutic Uses.—The application of heat to the entire body is used where the bodily temperature has fallen, or is likely to fall, very low, as in the algid stage of cholera, and in infants born prematurely. The *general* application of heat is obtained by use of warm baths, packing, vapour baths, and the copious use of hot drinks. The *local* application of heat is obtained by the use of warm wrappings, partial baths, plunging the parts in warm earth or sand or placing wounded parts in chambers filled with heated air. After removal of the heating agent, care must be taken to prevent a great escape of heat due to the dilatation of the blood-vessels.

223. INCREASE OF TEMPERATURE POST-MORTEM.—**Phenomena.**—Heidenhain found that in a dead dog, before the body cooled, there was a constant temporary rise of the temperature, which slightly exceeded the normal. The same observation had been occasionally made on human bodies immediately after death, especially when death was preceded by muscular spasms [also in yellow fever]. Thus Wunderlich measured the temperature fifty-seven minutes after death in a case of tetanus, and found it to be 45.375°C .

Causes.—(1) *A temporary increased production of heat after death*, due chiefly to the change of the semi-solid myosin of the muscles into a solid form (rigor mortis). As the muscle coagulates, heat is produced. All conditions which cause rapid and intense coagulation of the muscles—e.g., spasms—favour a *post-mortem* rise of temperature (see § 295); a rapid coagulation of the blood has a similar result (§ 28, 5).

(2) Immediately after death a series of *chemical processes* occur within the body, whereby heat is produced. Valentini placed a dead rabbit in a chamber, so that no heat could be given off from the body, and he found that the internal temperature of the animal's body was increased. The processes which cause a rise of temperature *post-mortem* are more active during the first than the second hour; and the higher the temperature at the moment of death, the greater is the amount of heat evolved after death.

(3) Another cause is the *diminished excretion of heat post-mortem*. After the circulation is abolished, within a few minutes little heat is given off from the surface of the body, as rapid excretion implies that the cutaneous vessels must be continually filled with warm blood.

224. ACTION OF COLD ON THE BODY.—**Phenomena.**—A short temporary slight cooling of the skin (removing one's clothes in a cool room, a cool bath for a short time, or a cool douche) causes either no change or a slight rise in the bodily temperature. The slight rise when it occurs is due to the stimulation of the skin, causing reflexly a more rapid molecular transformation, and therefore a greater production of heat, while the amount of heat given off is diminished owing to contraction of the small cutaneous vessels and the skin itself (*Liebermeister*). The continuous and intense application of cold causes a decrease of the temperature, chiefly by conduction, notwithstanding that at the same time there is a greater production of heat. After a cold bath the temperature may be 34° , 32° , and even 30° .

As an *after-effect* of the great abstraction of heat, the temperature of the body after a time remains lower than it was before ("*primary after-effect*"—*Liebermeister*); thus after an hour it was 0.22°C . less in the rectum. There is a "*secondary after-effect*" which occurs after the first after-effect is over, when the temperature rises (*Jürgensen*). This effect begins five to eight hours after a cold bath, and is equal to $+0.2^{\circ}\text{C}$. in the rectum. Hoppe-Seyler found that some time after the application of heat there was a corresponding lowering of the temperature.

Taking Cold.—If a rabbit be taken from a surrounding temperature of 35°C ., and suddenly cooled, it shivers, and there may be diarrhoea. After two days the temperature rises 1.5°C ., and albuminuria occurs. There are microscopic traces of interstitial inflammation in the kidneys, liver, lungs, heart, and nerve-sheaths, the dilated arteries of the liver and lung contain thrombi, and in the neighbourhood of the veins are accumulations of leucocytes. In pregnant animals, the fetus shows the same conditions. Perhaps the greatly cooled blood acts as an irritant causing inflammation.

Action of Frost.—The continued application of a high degree of cold causes at first contraction of the blood-vessels of the skin and its muscles, so that it becomes pale. If continued, paralysis of the cutaneous vessels occurs, the skin becomes red owing to congestion of its vessels. As the passage of fluids through the capillaries is rendered more difficult by the cold, the blood stagnates, and the skin assumes a *livid appearance*, as the O is almost completely used up. Thus the peripheral circulation is slowed. If the action of the cold be still more intense, the peripheral circulation stops completely, especially in the thinnest and most exposed

organs—ears, nose, toes, and fingers. The sensory nerves are paralysed, so that there is numbness with loss of sensibility, and the parts may even be frozen through and through. As the slowing of the circulation in the superficial vessels gradually affects other areas of the circulation, the pulmonary circulation is enfeebled, and diminished oxidation of the blood occurs, notwithstanding the greater amount of O in the cold air, so that the *nerve centres* are affected. Hence arise great dislike to making movements or any muscular effort, a painful sensation of fatigue, a peculiar and almost irresistible desire to sleep, cerebral inactivity, blunting of the sense-organs, and lastly, coma. The blood freezes at -3.9°C ., while the juices of the superficial parts freeze sooner. Too rapid movements of the frost-bitten parts ought to be avoided. Rubbing with snow, and the very gradual application of heat, produce the best results. Partial death of a part is not unfrequently produced by the prolonged action of cold.

225. ARTIFICIAL LOWERING OF THE TEMPERATURE.—Phenomena.

—The artificial cooling of warm-blooded animals, by placing them in cold air or in a freezing mixture, gives rise to a series of characteristic phenomena. If the animals (rabbits) are cooled so that the temperature (rectum) falls to 18° , they suffer great depression, without, however, the voluntary or reflex movements being abolished. The *pulse* falls from 100 or 150 to 20 beats per minute, and the blood-pressure falls to several millimetres of Hg. The *respirations* are few and shallow. Suffocation does not cause spasms, the secretion of urine stops, and the liver is congested. The animal may remain for twelve hours in this condition, and when the muscles and nerves show signs of paralysis coagulation of the blood occurs after numerous blood-corpuscles have been destroyed. The retina becomes pale, and death occurs with spasms and the signs of asphyxia. If the bodily temperature be reduced to 17° and under, the voluntary movements cease before the reflex acts. An animal cooled to 18°C ., and left to itself, at the same temperature as the surroundings, does not recover of itself, but if artificial respiration be employed, the temperature rises 10°C . If this be combined with the application of external warmth, the animals may recover completely, even when they have been apparently dead for forty minutes. Walther cooled adult animals to 9°C ., and recovered them by artificial respiration and external warmth; while Horvath cooled *young* animals to 5°C . Mammals, which are born blind, and birds which come out of the egg devoid of feathers, cool more rapidly than others. Morphine, and more so, alcohol, accelerate the cooling of mammals, at the same time the exchange of gases falls considerably; hence, drunk men are more liable to die when exposed to cold.

Artificial Cold-blooded Condition.—Cl. Bernard made the important observation, that the muscles of animals that had been cooled remained irritable for a long time to direct stimuli as well as to stimuli applied to their nerves; and the same is the case when the animals are asphyxiated for want of O. An “*artificial cold-blooded condition*,” i.e., a condition in which warm-blooded animals have a lower temperature, and retain muscular and nervous excitability, may also be caused in warm-blooded animals, by dividing the cervical spinal cord and keeping up artificial respiration; further, by moistening the peritoneum with a cool solution of common salt.

Hybernation presents a series of similar phenomena. Valentin found that hybernating animals become half awake when their bodily temperature is 28°C .; at 18°C . they are in a somnolent condition, at 6° they are in a gentle sleep, and at 1.6°C . in a deep sleep. The heart-beats and the blood-pressure fall, the former to 8 to 10 per minute. The respiratory, urinary, and intestinal movements cease completely, and the cardio-pneumatic movement alone sustains the slight exchange of gases in the lungs (§ 59). They cannot endure cooling to 0°C ., and awake before the temperature falls so low. Hybernating animals may be cooled to a greater degree than other mammals; they give off heat rapidly, and they become warm again rapidly, and even spontaneously. New-born mammals resemble hybernating animals more closely in this respect than do adults.

Cold-blooded animals may be cooled to 0° . Even when the blood has been frozen and ice formed in the lymph of the peritoneal cavity, frogs may recover. In this condition they appear to be dead, but when placed in a warm medium they soon recover. A frog's muscle so cooled will contract again. The germs and ova of lower animals, e.g., insects' eggs, survive continued

frost; and if the cold be moderate, it merely retards development. Bacteria, *e.g.*, *Bacillus anthracis*, survive a temperature of -130°C .; yeast, even -100°C .

Varnishing the skin causes a series of similar phenomena. The varnished skin gives off a large amount of heat by radiation, and sometimes the cutaneous vessels are greatly dilated. Hence the animals cool rapidly and die, although the consumption of O is not diminished. If cooling be prevented by warming them and keeping them in warm wool, the animals live for a longer time. The blood *post-mortem* does not contain any poisonous substances, nor even are any materials retained in the blood which can cause death, for if the blood be injected into other animals, these remain healthy.

226. EMPLOYMENT OF COLD.—Cold may be applied to the whole or part of the surface of the body in the following conditions:—

(a) By placing the body for a time in a **cold bath** to abstract as much heat as possible, when the bodily temperature in fever rises so high as to be dangerous to life. This result is best accomplished and lasts longest when the bath is gradually cooled from a moderate temperature. If the body be placed at once in cold water, the cutaneous vessels contract, the skin becomes bloodless, and thus obstacles are placed in the way of the excretion of heat. A bath gradually cooled in this way is borne longer. The addition of stimulating substances, *e.g.*, salts, which cause dilation of the cutaneous vessels, facilitates the excretion of heat; even salt water conducts heat better. If alcohol be given internally at the same time it lowers the temperature.

(b) Cold may be applied **locally** by means of ice in a bag, which causes contraction of the cutaneous vessels and contraction of the tissues (as in inflammation), while at the same time heat is abstracted locally.

(c) Heat may be abstracted locally by the **rapid evaporation** of volatile substances (ether, carbon disulphide), which causes numbness of the sensory nerves. The introduction of media of low temperature into the body, respiring cool air, taking cold drinks, and the injection of cold fluids into the intestine act locally, and also produce a more general action. In applying cold it is important to notice that the initial contraction of the vessels and the contraction of the tissues are followed by a greater dilatation and turgescence, *i.e.*, by a healthy reaction.

227. HEAT OF INFLAMED PARTS.—“**Calor**,” or heat, is reckoned one of the fundamental phenomena of inflammation, in addition to **rubor** (redness), **tumor** (swelling), and **dolor** (pain). But the apparent increase in the heat of the inflamed parts is not above the temperature of the blood. Simon, in 1860, asserted that the arterial blood flowing to an inflamed part was cooler than the part itself, but this has been contradicted. The outer parts of the skin in an inflamed part are warmer than usual, owing to the dilatation of the vessels (rubor) and the consequent acceleration of the blood-stream in the inflamed part, and, owing to the swelling (tumor), from the presence of good heat-conducting fluids; but the heat is not greater than the heat of the blood. It is not proved that an increased amount of heat is produced owing to increased molecular decompositions within an inflamed part.

228. HISTORICAL AND COMPARATIVE.—According to Aristotle, the heart prepares the heat within itself, and sends it along with the blood to all parts of the body. This doctrine prevailed in the time of Hippocrates and Galen, and occurs even in Cartesius and Bartholinus (1667,¹ “*flammula cordis*”). The **iatro-mechanical school** (*Boerhave, van Swieten*) ascribed the heat to the friction of the blood on the walls of the vessels. The **iatro-chemical school**, on the other hand, sought the source of heat in the fermentations that arose from the passage of the absorbed substances into the blood (*van Helmont, Sylvius, Ettmüller*). Lavoisier (1777) was the first to ascribe the heat to the combustion of carbon in the lungs. After the construction of the **thermometer** by Galileo, Sanctorius (1626) made the first thermometric observations on sick persons, while the first *calorimetric* observations were made by Lavoisier and Laplace. **Comparative** observations are given at § 207, and also under *Hibernation* (§ 225).

Physiology of the Metabolic Phenomena, &c.

By the term **metabolism** we mean those phenomena, whereby all—even the most lowly—living organisms are capable of incorporating the substances obtained from their food into their tissues, and making them an integral part of their own bodies. This part of the process is known as **assimilation**. Further, the organism in virtue of its metabolism forms a store of potential energy, which it can transform into *kinetic energy*, and which, in the higher animals at least, appears most obvious in the form of muscular work and heat. The **changes of the constituents of the tissues**, by which these transformations of the potential energy are accompanied, result in the formation of **excretory products**, which is another part of the process of metabolism. The normal metabolism requires the supply of food quantitatively and qualitatively of the proper kind, the laying up of this food within the body, a regular chemical transformation of the tissues, and the formation of the effete products which have to be given out through the excretory organs. [Synthetic or constructive metabolism is spoken of as **anabolic**, and destructive or analytical metabolism as **katabolic**, metabolism.]

[The human organism is continually giving off daily, *i.e.*, **daily losses**:—

By the **lungs**: carbon dioxide and watery vapour.

By the **kidneys**: water, urea, uric acid, &c., and salts.

By the **skin**: water, and a small quantity of CO₂ and fatty matter.

By the **bowel**: water, insoluble salts and residues of food, &c.

From the surfaces of the body are given off a small quantity of epithelium and mucus, and, under certain conditions, the products of the secretion of the mammary glands and testes.

The organism takes in daily a certain amount of matter, *i.e.*, **daily gains**.

By the **lungs**: oxygen.

By the **digestive tract**, *i.e.*, food: water, salts, proteids, carbohydrates, and fats.

When the income exactly equals the expenditure, *i.e.*, quantitatively, the animal is said to be **in equilibrium**.]

[We have discussed the daily income and expenditure of the body from the quantitative side, but when we compare these **qualitatively** we find that there is a great difference between what we take in as food and give off as excretions. Setting aside the water and salts taken in with the food—for they are excreted nearly unchanged—our food consists of highly complex organic, and but slightly oxidised bodies—**proteids, fats, and carbohydrates**; while the **excreta**, on the other hand, are such simple bodies as **carbon dioxide (CO₂), water, and urea**, the last of which readily splits up into carbon dioxide and ammonia. We have seen that a supply of oxygen is absolutely necessary for life, and that it is taken in by the respiratory processes, and carried to the tissues by the hæmoglobin of the red blood-corpuscles. In the capillaries these give up their oxygen to the

tissues, and we have seen good reasons for believing that the oxygen is used up in the tissues themselves—**oxidation-processes**—and that there also carbon dioxide is formed (§ 131), constituting the so-called “inner respiration.” In the tissues and organs the nutrient organic substances are more and more oxidised, until the final products, water, carbon dioxide, and urea are reached. All this takes place through and by the activity of the living cellular elements of the tissues. The cellular elements of each organ or tissue select from the lymph the materials they require, but it is evident that the process of oxidation in the tissues is not determined solely by their affinity for oxygen, for the fats which are oxidised with difficulty are completely decomposed in the body into CO_2 and H_2O . Again, such easily oxidisable substances as uric acid occur in the body, while some substances which are greedy of oxygen, *e.g.*, pyrocatechin, pass into the urine unchanged.]

[But we have every reason to believe that **reduction-processes** also take place in the organism, although they are far less than the oxidation-processes. When we group the various chemical processes taking place in the body, they are by no means all simple processes of oxidation; we have **dissociation**, or the separation of a complex body into its components, taking place, as in the separation of HbO_2 into Hb and O. The decomposition may be either of a simple nature, *i.e.*, without the addition of any new element,—*i.e.*, **simple decomposition**,—or a molecule of water may be taken up, constituting **hydrolytic decomposition**, or oxygen may be combined with it, constituting what we know as **oxidation**. In addition, various synthetic and reduction-processes may take place; so that it is plain that decomposition and oxidation-processes go on together in the organism.]

[When we compare the complex proteid with what represents it chiefly in the excreta—*viz.*, urea—one is not to assume that urea is formed directly from the proteid. There is reason to believe that in the process of katabolism there are a large number of intermediate less highly oxidised bodies formed before the final stage of urea is reached. We are but imperfectly acquainted with these. The following represents some of these bodies, as far as their ratio of C and N are concerned, but one is not to assume that they are all precursors of urea.

Albumin	contains 1 atom N to 4 C			
Glutin	“	1	“	$3\frac{1}{8}$ “
Glycin	“	1	“	2 “
Kreatin and Kreatinin	“	1	“	$1\frac{1}{3}$ “
Uric acid	“	1	“	$1\frac{1}{4}$ “
Allantoin	“	1	“	1 “
Urea	“	1	“	$\frac{1}{2}$ “

In proportion as the members of this group become poorer in C, they become richer in N, and also in O.]

[Of the numerous intermediate bodies—the products of the retrogressive metabolism of the tissues—we know much too little to be able to state definitely what are the immediate precursors of urea. Perhaps leucin, glyecoll or glycin, asparagin and ammonia salts are precursors of urea; at least when given to an animal they reappear as urea. These bodies, as we have seen, are formed in the small intestine, and it is supposed that they are changed into urea in the liver (§ 256).]

[As albumin contains 1 atom N to 4 C and urea 1 N to $\frac{1}{2}$ C, it is evident that in the decomposition of a proteid a non-nitrogenous residue must be set free, and doubtless it also forms a series of intermediate bodies, each of which step by step gains more O, and contains less C, until it is finally excreted as CO_2 and H_2O . If, however, the amount of this non-nitrogenous residue be greater than can be decomposed in the body, there is reason to believe that it may be stored up in the form of fat (§ 241).]

[The changes undergone by the **carbohydrates** are much simpler. First the

starches are changed into sugar in the mouth and intestine, and sugar formed in the intestine enters the blood for the most part as such. In the liver it is dehydrated and glycogen is formed, but this again slowly enters the blood-stream as sugar. It is then comparatively rapidly oxidised into CO_2 and H_2O . What the intermediate products are is uncertain. If the sugar be in excess of the needs of the economy it is supposed that it may be stored up as fat (§ 241).]

[The **fats**, although they are decomposed with difficulty by oxidising agents, are yet rapidly and completely split up in the organism into CO_2 and H_2O . The oxidation does not seem to be a direct process, but a number of intermediate bodies seem to be formed. We have in the body examples of the series of fatty acids with the formula $\text{C}_n\text{H}_{2n}\text{O}_2$ (formic, acetic, propionic acid, &c.) so that they are probably intermediate bodies. When fat is taken in excess it is not necessarily stored up in the body; in fact, there is reason to believe that fat in the body is chiefly formed from proteids (§ 241).]

[Amongst the **oxidation** processes may be classified the formation of **sulphuric acid**. The sulphur contained in the proteid molecule is oxidised, and appears either as a sulphate, or, in small amount, in the aromatic compounds of the urine (§ 262) (After *Munk*).]

["The chemical processes of the animal organism, therefore, may be represented as a series of oxidation and reduction processes,—chiefly, however, analytical processes—in virtue of which the highly complex and slightly oxidised constituents of the body, *i.e.*, those taken into the body as food—are decomposed into the simple and highly oxidised compounds—urea, carbon dioxide, sulphuric acid, and water, and removed from the body as such by the various organs of excretion" (*Munk*).]

[Alongside of these oxidation processes there are certain **synthetic** and **reduction processes** which take place in the body, *e.g.*, the formation of hæmoglobin. Benzoic acid unites with glycocholic acid, and appears in the urine as hippuric acid (§ 260); phenol unites with sulphuric acid, and appears as phenol-sulphuric acid. Fatty acids taken into the alimentary canal unite somewhere with glycerin and form the corresponding neutral fat (§ 192, 3), and this without glycerin being administered at the same time with the fatty acid. But, in any case, the synthetic processes are far less in evidence, and are far fewer in number, than the oxidation and analytic chemical processes, which are so characteristic of animal metabolism generally, in contrast to what occurs in vegetable metabolism (see *Introduction*).]

229. THE MOST IMPORTANT SUBSTANCES USED AS FOOD.—Water.

—When we remember that 58·5–64 per cent. of the body consists of water, that water is being continually given off by the urine and fæces, as well as through the skin and lungs, that the processes of digestion and absorption require water for the solution of most of the substances used as food, and that numerous substances excreted from the body require water for their solution, especially in the urine, the great importance of water and its continual renewal within the organism are at once apparent. As put by Hoppe-Seyler, all organisms live in water, and even in running water, a remark which ranks with the old saying—"Corpora non agunt nisi fluida."

[According to Volkmann, 100 parts of a human being consist of 64 parts water 16 proteid (and gelatin), 14 fat, and 5 parts ash. As the muscles make up 42–43 parts of the entire body, and contain 21 per cent. of proteid and 75 per cent. of water, it is evident that in round numbers the muscles contain about half the proteids and more than the half of the total water of the body.]

Water—as far as it is not a constituent of all fluid foods—occurs in different forms as drink:—(1) **Rain water**, which most closely resembles distilled or chemically pure water, always contains minute quantities of CO_2 , NH_3 , nitrous and nitric acids. (2) **Spring water** usually contains much mineral substance. It is formed from the deposition of watery vapour or rain from the air, which permeates the soil, containing much CO_2 ; the CO_2 is dissolved by the

water, and aids in dissolving the alkalis, alkaline earths, and metals, which appear in solution as bicarbonates, *e.g.*, of lime or iron oxide. The water is removed from the spring by proper mechanical appliances, or it bubbles up on the surface in the form of a "spring." (3) **River water** usually contains much less mineral matter than spring water. Spring water floating on the surface rapidly gives off its CO_2 , whereby many substances—*e.g.*, lime—are thrown out of solution, and deposited as insoluble precipitates.

Gases in water.—Spring water contains little O, but much CO_2 , the latter giving to it its fresh taste. Hence, vegetable organisms flourish in spring water, while animals requiring, as they do, much O, are but poorly represented in such water. Water flowing freely gives up CO_2 , and absorbs O from the air, and thus affords the necessary conditions for the existence of fishes and other marine animals. River water contains $\frac{1}{30}$ to $\frac{1}{20}$ of its volume of absorbed gases, which may be expelled by boiling or freezing.

Drinking water is chiefly obtained from springs. River water, if used for this purpose, must be filtered to get rid of mechanically suspended impurities. For household purposes a charcoal filter may be used, as the charcoal acts as a disinfectant. **Alum** has a remarkable action. When added to give a dilution containing 0.0001 per cent., it makes turbid water clear.

Investigation of Drinking Water.—Drinking water, even in a thick layer, ought to be completely *colourless, not turbid, and without odour*. Any odour is best recognised by heating it to 50°C ., and adding a little caustic soda. It ought not to be *too hard*, *i.e.*, it ought not to contain too much lime (and magnesia) salts.

By the term "**degree of hardness**" of a water is meant the unit amount of lime (and magnesia) in 100,000 parts of water; a water of 20 degrees of hardness contains 20 parts of lime (calcium oxide) combined with CO_2 , sulphuric, or hydrochloric acids (the small amount of magnesia may be neglected). *A good drinking water ought not to exceed 20 degrees of hardness.* The hardness is determined by titrating the water with a standard soap solution, the result being the formation of a scum of lime-soap on the surface. The hardness of *unboiled* water is called its *total hardness*, while that of *boiled water* is called **permanent hardness**. Boiling drives off the CO_2 , and precipitates the calcium carbonate, so that the water at the same time becomes softer.

The presence of **sulphuric acid**, or sulphates, is determined by the water becoming turbid on adding a solution of barium chloride and hydrochloric acid.

Chlorine occurs in small amount in pure spring water, but when it occurs there in large amount—apart from its being derived from saline springs, near the sea or manufactories—we may conclude that the water is contaminated from water-closets or dunghills, so that the estimation of chlorine is of importance. For this purpose use a solution, A, of 17 grms. of crystallised silver nitrate in 1 litre of distilled water; 1 cubic centimetre of this solution precipitates 3.55 milligrams of chlorine as silver chloride. Use also B, a cold saturated solution of neutral potassium chromate. Take 50 cubic centimetres of the water to be investigated, and place it in a beaker, add to it 2 to 3 drops of B, and allow the fluid A to run into it from a burette until the white precipitate first formed *remains* red, even after the fluid has been stirred. Multiply the number of cubic centimetres of A used by 7.1, and this will give the amount of chlorine in 100,000 parts of the water. **Example**—50 c.centr. requires 2.9 c.centr. of the silver solution, so that 100,000 parts of the water contain $2.9 \times 7.1 = 20.59$ parts chlorine (*Kubel Tiemann*). Good water ought not to contain more than 15 milligrams of chlorine per litre.

The presence of **lime** may be ascertained by acidulating 50 cubic centimetres of the water with HCl, adding ammonia in excess, and afterwards adding ammonia oxalate; the white precipitate is lime oxalate. According to the degree of turbidity, we judge whether the water is "**soft**" (poor in lime), or "**hard**" (rich in lime).

Magnesia is determined by taking the clear fluid of the above operation, after removing the precipitate of lime, and adding to it a solution of sodium phosphate and some ammonia; the crystalline precipitate which occurs is magnesia.

The more feeble all these reactions which indicate the presence of sulphuric acid, chlorine, lime, and magnesia are, the better is the water. In addition, good water ought not to contain more than traces of nitrates, nitrites, or compounds of ammonia, as their presence indicates the decomposition of nitrogenous organic substances.

For **nitric acid**, take 100 cubic centimetres of water acidulated with two or three drops of concentrated sulphuric acid, add several pieces of zinc together with a solution of potassium iodide, and starch solution—a blue colour indicates nitric acid. The following tests are very delicate:—(1) **Brucine test**.—Add to half a drop of water in a capsule two drops of a watery solution of Brucinum sulphuricum, and afterwards several drops of concentrated sulphuric acid; a rose-red coloration indicates the presence of nitric acid. (2) [**Diphenylamine test**.—Pour a thin layer of a 2 per cent. solution of diphenylamine in strong sulphuric acid on a white plate. A drop of water containing nitrates or nitrites gives a blue colour.]

The presence of **nitrous acid** is ascertained by the blue coloration which results from the

addition of a solution of potassium iodide, and solution of starch, after the water has been acidulated with sulphuric acid.

Compounds of ammonia are detected by Nessler's reagent, which gives a yellow or reddish coloration when a trace of ammonia is present in water; while a large amount of these compounds gives a brown precipitate of the iodide of mercury and ammonia.

The **contamination of water** by decomposing animal substance is determined by the amount of N it contains. In most cases it is sufficient to determine the amount of *nitric acid* present. For this purpose we require (A) a solution of 1.871 grms. potassium nitrate in one litre distilled water—1 cubic centimetre contains 1 milligram nitric acid; (B) a dilute solution of indigo, which is prepared by rubbing together one part of pulverised indigotin with six parts H_2SO_4 , and allowing the deposit to subside, when the blue fluid is poured into forty times its volume of distilled water and filtered. This fluid is diluted with distilled water until a layer, 12 to 15 mm. in thickness, begins to be transparent.

To test the activity of B, place 1 cubic centimetre of A in 24 cubic centimetres water, add some common salt and 50 cubic centimetres concentrated sulphuric acid, and allow B to flow from a burette into this mixture until a faint green colour is obtained. The number of cubic centimetres of B used correspond to 1 milligram of nitric acid.

Twenty-five cubic centimetres of the water to be investigated are mixed with 50 cubic centimetres of concentrated H_2SO_4 , and titrated with B until a green colour is obtained. This process must be repeated, and on the second occasion the solution B must be allowed to flow in at once, when usually somewhat more indigo solution is required to obtain the green solution. The number of cubic centimetres of B (corresponding to the strength of B as determined above) indicates the amount of nitric acid present in 25 c.cmtr. of the water investigated. As much as 10 milligrams nitric acid have been found in spring water (*Marx, Trommsdorff*).

Sulphuretted Hydrogen is recognised by its *odour*; also by a piece of blotting-paper moistened with alkaline solution of lead becoming brown, when it is held over the boiling water. If it occurs as a *compound* in the water, sodium nitro-prusside gives a reddish-violet colour.

It is of the greatest importance that drinking water should be *free from the presence of organic matter* in a state of decomposition. Organic matter in a state of decomposition, and the organisms therewith associated, when introduced into the body, may give rise to fatal maladies, *e.g.*, cholera and typhoid fever. This is the case when the water-supply has been contaminated from water which has percolated from water-closets, privies, and dung-pits. *The presence of organic matter may be detected thus*—(1) A considerable amount of the water is evaporated to dryness in a porcelain vessel; if the residue be heated again a brown or black colour indicates the presence of a considerable amount of organic matter; and if it contain N, there is an odour of ammonia. Good water treated in this way gives only a light brown stain. The presence of **micro-organisms** may be determined microscopically after evaporating a small quantity of the water on a glass slide. (2) The addition of *potassio-gold chloride* to the water gives a black frothy precipitate after long standing. (3) A solution of *potassium permanganate*, added to the water in a covered jar, gradually becomes decolorised, and a brownish precipitate is formed.

Water containing much organic matter should *never* be used as drinking water, and this is especially the case when there is an epidemic of typhoid fever, cholera, or diarrhœa. In all such circumstances, the water ought to be boiled for a long time, whereby the organic germs are killed. The insipid taste of the water after boiling may be corrected by adding a little sugar or lime juice.

230. THE MAMMARY GLANDS AND MILK.—Milk-Duct.—About 20 galactiferous ducts open singly upon the surface of the nipple. Each of these, just before it opens on the surface, is provided with an oval dilatation—the **sinus lacteus**. When traced into the gland, the galactiferous ducts divide like the branches of a tree, and a large branch of the duct passes to each **lobe** of the gland, all the lobes being held together by loose connective-tissue. Only during lactation do all the fine terminations of the ducts communicate with the globular glandular acini. Every gland **acinus** consists of a *membrana propria*, surrounded externally with a network of branched connective-tissue corpuscles, and lined internally with a somewhat flattened polyhedral layer of nucleated **secretory cells** (fig. 287). The size of the lumen of the acini depends upon the secretory activity of the glands; when it is large, it is filled with milk containing numerous refractive fatty granules. The walls of the milk-ducts consist of fibrillar connective-tissue. Some fibres are arranged longitudinally, but the chief mass are disposed circularly, and are permeated externally with elastic fibres, while in the finer ducts there is a *membrana propria* continuous with that of the gland acini. The ducts are lined by cylindrical epithelium.

During the *first few days after delivery*, the breasts secrete a small amount of milk of greater consistence, and of a yellow colour—the **colostrum**—in which large cells filled with fatty granules occur—the colostrum-corpuscles (fig. 289). Sometimes a nucleus is observable within them, and rarely they exhibit amœboid movements (fig. 288, *c, d, e*). The regular secretion of milk begins after three to four days. It was formerly supposed that the cells of the acini underwent a fatty degeneration, and thus produced the fatty granules of the milk. It is more probable, from recent observations, that the cells of the acini manufacture the fatty granules, and their protoplasm eliminates them, at the same time forming the clear fluid part of the milk.

Changes in the gland cells during Secretion.—Pratsch and Heidenhain found that the secretory cells in the **non-secreting gland** (fig. 288, I), were flat, polyhedral, and uni-nucleated, whilst the **secreting cells** (fig. 288, II) often contained several nuclei, were more albuminous, higher, and cylindrical in form. The edge of the cell directed towards the lumen of the acinus undergoes characteristic changes during secretion. Fatty granules are formed in this part of the cell, and are afterwards extruded. The decomposed portion of the cell is dissolved in the milk, and the fatty granules become free as milk-globules (fig. 288, II. *a*). If nuclei are present

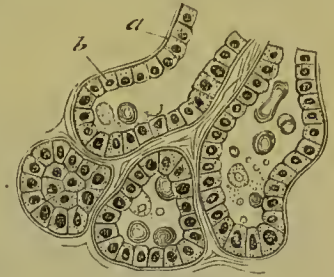


Fig. 287.

Acini of the mammary gland of a sheep during lactation. *a*, membrana propria; *b*, secretory epithelium.



Fig. 288.

I. Inactive acinus of the mamma. II. During the secretion of milk—*a, b*, milk-globules; *c, d, e*, colostrum corpuscles; *f*, pale cells (bitch).

in that part of the cell which is broken up, they also pass into the milk and give rise to the presence of nuclein in the secretion.

Besides the milk-globules and colostrum corpuscles, Rauber has found leucocytes undergoing fatty degeneration, and single pale cells (*f*). Occasionally milk-globules are found with traces of the cell-substance adhering to their surface (*b*).

Formation of Milk.—Concerning the formation of the individual constituents of milk, H. Thierfelder, who digested fresh mammary glands directly after death, found that during the digestion of the glands, at the temperature of the body, a reducing substance, probably **lactose**, was formed by a process of fermentation. The mother substance (sacliarogen) is soluble in water, but not in alcohol or ether, is not destroyed by boiling, and is not identical with glycogen. The ferment which forms the lactose is connected with the gland-cells—it does not pass into the milk, nor into a watery extract of the gland. During the digestion of the mammary glands at the temperature of the body, **casein** is formed, probably from serum-albumin, by a process of fermentation. This ferment occurs in the milk.

The **nipple** and its **areola** are characterised by the presence of pigment—more abundant during pregnancy—in the rete Malpighii of the skin, and by large papillae in the *entis vera*. Some of the papillae contain touch-corpuscles. Numerous non-striped muscular fibres surround the milk-ducts in the deep layers of the skin and in the subcutaneous tissue, which contains no fat. These muscular fibres can be traced, following a longitudinal course, to the termination of

the ducts on the surface. The small glands of Montgomery, which occur on the areola during lactation, are just small milk-glands, each with a special duct opening on the surface of the elevation.

Arteries proceed from several sources to supply the mamma, but their branches do not accompany the milk-ducts; each gland acinus is surrounded by a network of *capillaries*, which communicate with those of adjoining acini by small arteries and veins. The veins of the areola are arranged in a circle (circulus Halleri). The **nerves** are derived from the supraclavicular, and the II–IV–VI intercostals; they proceed to the skin over the gland, to the very sensitive nipple, to the blood-vessels and non-striped muscle of the nipple, and to the gland acini, where their mode of termination is still unknown. **Lymphatics** surround the alveoli, and they are often full. The milk appears to be prepared from the lymph contained in the lymphatics surrounding the acini.

Comparative anatomy of the mamma.—The rodents, insectivora, and carnivora have 10 to 12 teats, while some of them have only 4. The pachydermata and ruminantia have 2 to 4 abdominal teats, the whale has 2 near the vulva. The apes, bats, vegetable-feeding whales, elephants, and sloths have 2, like man. In the marsupials the tubes are arranged in groups, which open on a patch of skin devoid of hair without any nipple. The young animals remain within the mother's pouch, and the milk is expelled into their mouths by the action of a muscle—the compressor mammae.

The development of the human mamma begins in both sexes during the third month; at the fourth and fifth months a few simple tubular gland-ducts are arranged radially around the position of the future nipple, which is devoid of hair. In the new-born child the ducts are branched twice or thrice, and are provided with dilated extremities, the future acini. Up to the twelfth year, in both sexes, the ducts continue to divide dendritically; but without any proper acini being formed. In the girl at puberty, the ducts branch rapidly; but the acini are formed *only at the periphery* of the gland; during pregnancy, acini are also formed in the centre of the gland, while the connective-tissue at the same time becomes somewhat more opened out. At the climacteric period, or menopause, all the acini and numerous fine milk-ducts degenerate. In the *adult male*, the gland remains in the non-developed infantile condition. Accessory or supernumerary glands upon the breast and abdomen are not uncommon, sometimes the mamma occurs in the axilla, on the back, over the acromion process, or on the leg. A slight secretion of milk in a newly-born infant is normal.

During the **evacuation of the milk** (500–1500 cubic centimetres daily), there is not only the mechanical action of sucking, but also the activity of the gland itself (§ 152). This consists in the erection of the nipple, whereby its non-striped muscular fibres compress the sinuses on the milk-ducts, and empty them, so that the milk may flow out in streams. The gland acini are also excited to secretion reflexly by the stimulation of the **sensory nerves** of the nipple. The vessels of the gland are dilated, and there is a copious transudation into the gland—the transuded fluid being manufactured into milk under the influence of the secretory protoplasm. The amount of secretion has a relation to the blood-pressure (*Röhrig*). During sucking, not only is the milk in the gland extracted, but new milk is formed, owing to the accelerated secretion. Emotional disturbances—anger, fear, &c.—arrest the secretion. Laffont found that stimulation of the mammary nerve (biteh) caused erection of the teat, dilatation of the vessels, and secretion of milk. After section of the cerebro-spinal nerves going to the mamma, Eekhard observed that erection of the teat ceased, although the secretion of milk in a goat was not interrupted. The rarely observed **galactorrhœa** is perhaps to be regarded as a paralytic secretion analogous to the paralytic secretion of saliva. Heidenhain and Pratsch found that the secretion (biteh) was increased by injecting strychnine or curare after section of the nerves of the gland. The “**milk-fever**,” which accompanies the first secretion of milk, probably depends on stimulation of the vaso-motor nerves, but this condition must be studied in relation with the other changes which occur within the pelvic cavity after birth. [Some substances, such as atropin, arrest the secretion of milk.]

231. MILK AND ITS PREPARATIONS.—Milk represents a complete or typical food in which are present all the constituents necessary for maintaining the life and growth of the body of an infant (§ 236). [It contains 82–90 per cent. of water, and 10–18 per cent. of solids varying with the animal's milk investigated. In round numbers, the water = 87·5, proteid = 3·5, fats = 4, sugar = 5, and ash = 0·6. The solids of milk consist of proteids (chiefly casein or caseinogen), fats, carbohydrates (lactose), and inorganic salts.] [If an adult were to live on milk alone, to get the 23 oz. of dry solids necessary, he would have to take 9 pints of milk daily, which would give far too much water, fat, and proteids.] To every 10 parts of proteids there are 10 parts fat and 20 parts sugar. Relatively more of the fat than the proteid of the milk is absorbed (*Rubner*).

Characters.—Milk is an opaque, bluish-white fluid, with a sweetish taste and a characteristic odour, probably due to the peculiar volatile substances derived from the cutaneous secretions of the glands, and it has a specific gravity of 1026 to 1035. When it stands for a time, numerous milk globules, butter globules or **cream**, collect on its surface, under which there is a bluish watery fluid. Human milk is always *alkaline*, cow's milk may be alkaline, acid, or amphoteric; while the milk of carnivora is always slightly acid.

[**Quantity secreted.**—A woman secretes 800 cc. to 1 litre and a cow 6–7 litres per day.]

Milk-Globules.—When milk is examined *microscopically*, it is seen to contain numerous small highly refractive **oil-globules** [0.0015–0.005 millimetre in diameter], floating in a clear fluid—the **milk-plasma** (figs. 288, *a b*, 289); while colostrum corpuscles and epithelium from the milk-ducts are not so numerous. The white colour and opacity of the milk are due to the presence of the milk-globules, which reflect the light; the globules consist of a fat, or butter, and are said by some to be surrounded with a very thin envelope of *casein* or haptogen membrane [so that milk is a perfect **emulsion**.]

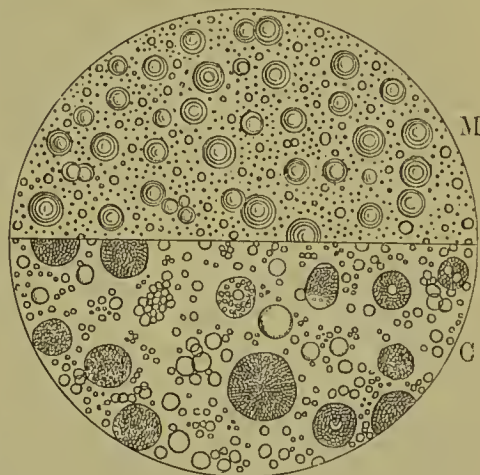


Fig. 289.

Microscopic appearance of milk, (M) upper half, and colostrum (C) lower half.

If acetic acid or liquor potassæ be added to a microscopic preparation of milk, the fatty granules run together to form irregular masses. If cow's milk be shaken with caustic potash, the casein envelopes are dissolved, and if ether be added, the milk becomes clear and transparent, as the ether dissolves out all the fatty particles in the solution. Ether cannot extract the fat from cow's milk until acetic acid or caustic potash is added to liberate the fats from their envelopes; but shaking with ether is sufficient to extract the fats from human milk. Some observers deny that an envelope of casein exists, and, according to them, milk is a simple emulsion, kept emulsified owing to the colloid swollen-up casein in the milk-plasma. The treatment of milk with potash and ether makes the casein unable any longer to preserve the emulsion (*Soxhlet*).

The **fats of the milk-globules** are the triglycerides of stearic, palmitic, oleic acids; very little myristic, arachic (butinic), capric, caprylic, caproic, and butyric acids, with traces of acetic and formic acids and cholesterin.

[The fats of milk exist in an emulsified condition, but even the finest milk-globules are much larger than the so-called molecular granules of chyle. The fats of milk are all animal fats, a mixture of olein, stearin, and palmitin, small quantities of capronin, and butyrin (tri-glycerides of caproic acid $C_6H_{12}O_6$ and butyric acid $C_4H_8O_2$). Their melting point is between 31 and 33° C. According to Lebedeff, human milk contains twice as much olein as palmitin and stearin, while in cow's milk they are about equal. Butyrin and capronin make up about $\frac{1}{14}$ of the fats of milk (*Munk*).]

Butter.—When milk is beaten or stirred for a long time (*i.e.*, churned), the fat of the milk-globules is ultimately obtained in the form of *butter*, owing to the rupture of the envelopes of casein. Butter is soluble in alcohol and ether, and it is clarified by heat (60° C.), or by washing in water at 40° C. When allowed to stand exposed to the air, it first becomes **sour**, owing to the formation of lactic acid, and afterwards **rancid**, owing to the glycerin of the neutral fats being decomposed by fungi into aerolein and formic acid, while the volatile fatty acids give it its rancid odour.

The **milk-plasma** is a clear, slightly opalescent fluid, and contains **casein** (§ 249, III. 3)—the chief proteid of milk—some **lact-albumin** (§ 32), small quantity of **nuclein**, and a trace of diastatic ferment (in human milk).

The presence of other peculiar chemical bodies, *e.g.*, lactoprotein, globulin, albumose, galactin, &c., is disputed by some chemists. Sebeliën distinguishes besides the above proteids **lacto-globulin**.

[**Proteids of Milk**.—There are two proteids in milk, one usually called **casein**, but which Halliburton proposes to call **caseinogen** (p. 299); this is the chief proteid and coagulates on the addition of rennet. The other is present in small amount and resembles serum-albumin in some characters, and is called **lact-albumin**.]

[**Caseinogen** may be precipitated by the addition of acids, or by saturating the milk with neutral salts, or, better still, by a combination of both methods. It is immediately clotted at 40° by rennet, but if it be washed to free it of all calcic phosphate, clotting does not then take place. Caseinogen is usually stated to resemble alkali-albumin, but the latter does not clot with rennin. In its behaviour towards neutral salts caseinogen behaves like a globulin.]

[**Casein**.—This name is restricted by Halliburton to the proteid formed by the action of rennin on caseinogen. It is insoluble in the whey, and is the chief constituent of cheese. Foster calls the coagulated casein **tyrein**.]

[**Lact-albumin** remains in solution after precipitation of caseinogen by $MgSO_4$. It coagulates at 70°–80°C, and is not separable by fractional heat-coagulation into several albumins.]

[**Lacto-globulin** is absent in normal milk although it is present in colostrum.]

[**Proteoses** and **peptones** are absent (*Halliburton*).]

When milk is **boiled** the albumin coagulates, while the surface also becomes covered with a thin scum or layer of casein, which has become insoluble [the rest of the milk remaining fluid. The scum is in part, perhaps, lact-albumin with altered caseinogen and some fat.]

Casein.—When milk is filtered through fresh animal membranes or through a clay filter [*i.e.*, through a porous clay cell under pressure], the *casein* does not pass through. [This shows that the casein is not in a state of true solution in the milk-plasma.] **Precipitation**.—It is precipitated by adding crystals of $MgSO_4$ to saturation. [If to milk twice its volume of a saturated solution of NaCl and crystals of NaCl be added, and the whole shaken thoroughly, casein is precipitated, and carries down with it fat, so that the clear filtrate contains the lactose, salts, and coagulable proteids.]

The plasma contains **milk-sugar** (§ 252) [which differs from dextrose chiefly in its much less solubility in water and alcohol, and its much less tendency to crystallise. Nor does it undergo the alcoholic fermentation directly]; a carbohydrate resembling dextrin, (? lactic acid), lecithin, urea, extractives, kreatin, sarkin, (potassic sulphocyanide in cow's milk), sodic and potassic chlorides, alkaline phosphates, calcium and magnesium sulphates, alkaline carbonates, traces of iron, fluorine, and silica; CO_2 , N, and O.

The **coagulation of milk depends upon the coagulation of its casein**, or, as it is called, *caseinogen*. In milk, caseinogen is combined with calcium phosphate, which keeps it in solution; acids which act on the calcium phosphate cause coagulation of the caseinogen (acetic and tartaric acids in excess redissolve it). All acids do not coagulate human milk. It is coagulated by two or more drops of hydrochloric acid (0.1 per cent.) or acetic acid (0.2 per cent.). The **spontaneous coagulation of milk** after it has stood for a time, especially in a warm place, is due to the production of **lactic acid**, which is formed from the milk-sugar in the milk by the action of *bacillus acidilactici* [which is introduced from without] (§ 184, 1.). It changes the neutral alkaline phosphate into the acid phosphate, takes the casein from the calcium phosphate, and precipitates the casein. The sugar is decomposed into lactic acid and CO_2 .

Souring of Milk.—When milk is exposed to the air for a time—varying with the temperature—it first becomes neutral, and then gradually acid; but for a time it remains fluid, even although acid. The acidity steadily increases, and after a certain degree of acidity the milk thickens, and finally a jelly-like mass is formed. This clot gradually shrinks—not unlike a blood clot—and squeezes out a small quantity of fluid, the **milk-serum**.

Rennet or rennin (§ 250, 9, *d*, § 166, 11.) coagulates milk with an *alkaline* reaction (sweet whey). This ferment **decomposes the caseinogen** into the precipitated cheese (**casein**) and also into the slightly soluble **whey-albumin**, so that the coagulation by rennet is a process quite

distinct from the coagulation of milk by the gastric and pancreatic juices, [and also from the precipitation produced by acids. The presence of calcium phosphate seems to be necessary for the complete action of the rennet (*Hammarsten*).]

[Experiments with rennet and milk.—Warm a little milk to 40° C., and add a few drops of commercial rennet, setting aside the mixture in a warm place; a solid coagulum is soon formed, and by and by the whey separates from it. If the milk be previously diluted with water, no coagulum is formed; and if the rennet be boiled before, it, like other ferments, is destroyed. A solution of rennet may be prepared by extracting the fourth stomach of the calf with glycerin. [When the milk is coagulated we obtain the **curd**, consisting of casein with some milk-globules entangled in it; the **whey** contains some soluble albumin and fat, and the great proportion of the salts and milk-sugar, together with lactic acid.]

[Under the influence of weak specimens of rennet ferment the casein of milk may not undergo a complete change to the more insoluble form of tyrcin (p. 299). The change may merely consist in certain chemical qualities of the casein being altered, the milk itself, as far as clotting or naked eye characteristics are concerned, being apparently unacted upon by the rennet ferment. The changes which the casein undergoes in these circumstances are that it becomes precipitated by a lower percentage of neutral salts or of free acid; whereas, under ordinary circumstances, there is no separation of casein by adding an equal bulk of saturated solution of sodium chloride to milk (there being required almost total saturation with the salt), yet under the above conditions an abundant separation of this changed casein occurs. With hydrochloric acid, just half the strength necessary to precipitate the casein in milk will form a curd when the milk has been subjected to such weak rennet ferment. One more point is of interest, and that is that the casein thus changed will coagulate on boiling, but for certain reasons this is not so satisfactory a test of the change as the action of neutral salt or free acid.

Pancreatic juice was long ago described as possessing a rennet ferment. Very strong specimens do not show this action, probably because the proteolytic action masks it, but less strong will give the above-mentioned characteristics though there may be no clotting of the milk as a whole. This power of the milk of becoming coagulated on boiling after treatment with pancreatic extracts was described first by Roberts as the **metacasein reaction** (*J. S. Edkins*).]

[A **milk-coagulating ferment** is found in certain plants (artichokes, figs, *Carica papaya*), and causes milk to coagulate in neutral or alkaline solutions. It is also found in the small intestine of the calf, while a 5 per cent. NaCl solution of the seeds of *Withania coagulans* coagulates milk in an alkaline medium.]

Boiling (by killing all the lower organisms), sodium bicarbonate ($\frac{1}{1000}$), ammonia, salicylic acid ($\frac{1}{5000}$), glycerin, and ethereal oil of mustard prevent the spontaneous coagulation. Fresh milk makes tincture of guaiacum blue, but boiled milk does not do so. When milk is exposed to the air for a long time, it gives off CO₂ and absorbs O; the fats are increased (? owing to the development of fungi in the milk), and so are the alcoholic and ethereal extracts from the decomposition of the casein. According to Schmidt-Mülheim, some of the casein becomes converted into peptone, but this occurs only in unboiled milk.

Composition.—100 parts of milk contain—

	Human.	Cow.	Goat.	Ass.
Water, ...	87.24 to 90.58	86.23	86.85	89.01
Solids, ...	9.42 „ 12.39	13.77	13.52	10.99
Casein, ...	2.91 „ 3.92	1.90 to 2.36 {	3.23	2.53
Albumin, ...	... „ ...		0.50	1.26
Butter, ...	2.67 „ 4.30		4.50	4.34
Milk-sugar, . . .	3.15 „ 6.09		4.93	3.78
Salts, ...	0.14 „ 0.28	0.61	0.65	5.05

[Cow's v. Human Milk.—The milk of the ass most closely resembles human milk, only the former contains much less fat. Cow's milk is $\frac{1}{3}$ richer in proteids, but $\frac{1}{7}$ – $\frac{1}{4}$ poorer in sugar. By adding $\frac{1}{4}$ vol. of water and sugar cow's milk can be made to resemble human milk. Human milk contains a very small amount of inorganic salts, its milk globules are smaller, and there are qualitative differences in its coagulated casein as compared with cow's milk. Cow's milk yields a dense curd, while the curd of human milk falls in a more flocculent condition; moreover, human milk is more easily digested both by normal and artificial gastric juice than cow's milk.]

[The following table shows the difference in composition between colostrum, (1–5 days after delivery) and milk (from the 7th day onwards).

In 100 parts.	Water.	Proteids.	Fats.	Sugar.	Salts.
Colostrum, ...	86.4	5.3	3.4	4.5	0.4
Milk, ...	87.8	2.5	3.9	5.5	0.3

Colostrum, therefore, is richer in solids, and the latter consist chiefly of albumin, and but little casein. The casein gradually increases at the expense of the albumin, and on the 7th day there is chiefly casein and little albumin. Colostrum contains less sugar.]

Gases.—Pflüger and Setschenow found in 100 vols. of milk 5.01 to 7.60 CO_2 ; 0.09 to 0.32 O; 0.70 to 1.41 N, according to volume. Only part of the CO_2 is expelled by phosphoric acid.

Salts.—The *potash salts* (as in blood-corpuscles and muscle are more abundant than the soda compounds, while there is a considerable amount of calcium phosphate, which is necessary for forming the bones of the infant. Wildenstein found in 100 parts of the ash of human milk—sodium chloride, 10.73; potassium chloride, 26.33; potash, 21.44; lime, 18.78; magnesia, 0.87; phosphoric acid, 19; ferric phosphate, 0.21; sulphuric acid, 2.64; silica, traces. The amount of salts present is affected by the salts of the food.

[Bunge gives the following table of the composition of the salts of milk :—

In 1000 parts.	Potash.	Soda.	Calcium.	Magnesia.	Iron oxide.	Phosphoric Acid.	Chlorine.
Woman's milk, . . .	0.7	0.3	0.3	0.1	0.006	0.5	0.4
Cow's milk, . . .	1.8	1.1	1.6	0.2	0.004	2.0	1.7

Conditions Influencing the Composition of Milk.—The oftener the breasts are *emptied*, the richer the milk becomes in casein. The last milk obtained at any time [“strippings”] is always richer in butter, as it comes from the most distant part of the gland—viz., the acini. Some substances are diminished and others increased in amount, according to the *time after delivery*. The following are *increased* :—Until the 2nd month after delivery, casein and fat; until the 5th month, the salts (which diminish progressively from this time onwards); from the 8th to the 10th month, the sugar. The following are *diminished* :—from 10th to 24th month, casein; from 5th to 6th and 10th to 11th month, fat; during 1st month, the sugar; from the 5th month, the salts.

The greater amount of milk that is secreted (woman), the more casein and sugar, and the less butter it contains. The milk of a primipara is less watery. Rich feeding, especially proteids (small amount of vegetable food), increases the amount of milk and the casein, sugar, and fat in it; a large amount of carbohydrates (not fats) increases the amount of sugar.

Modifying Conditions.—That cow's milk is influenced by the pasture and food is well known. Turnip as food gives a peculiar odour, taste, and flavour to milk, and so do the fragrant grasses. The mental state of the nurse influences the quantity and quality of the milk. Jaborandi is the nearest approach to a galactagogue, but its action is temporary. Atropin is a true anti-galactagogue. The composition of the milk may be affected by using fatty food, by the use of salts, and above all by the diet (*Dolan*).

[Milk may be a **vehicle for communicating disease**—by direct contamination from the water used for adulterating it or cleansing the vessels in which it is kept; by the milk absorbing deleterious gases; by the secretion being altered in diseased animals.] Milk ought not to be kept in zinc vessels, owing to the formation of zinc lactate.

Substitutes for Milk.—If other than human milk has to be used, ass's milk most closely resembles human milk. Cow's milk is best when it contains plenty of fatty matters—it must be diluted with its own volume of water at first and a little milk-sugar added. The casein of cow's milk differs qualitatively from that of human milk; its coagulated flocculi or curd are much coarser than the fine curd of human milk, and they are only $\frac{1}{4}$ dissolved by the digestive juices, while human milk is completely dissolved. Cow's milk when boiled is less digestible than unboiled milk.

Tests for Milk.—The amount of cream is estimated by placing the milk for twenty-four hours in a tall cylindrical glass graduated into a hundred parts, or **creamometer**; the cream collects on the surface, and ought to form from 10 to 24 vols. per cent. [The cream is generally about $\frac{8}{100}$.] The specific gravity (fresh cow's milk 1029 to 1034; when creamed, 1032 to 1040)—is estimated with the **lactometer** at 15° C. The sugar is estimated by titration with Fehling's solution (§ 150, II.), but in this case 1 cubic centimetre of the solution corresponds to 0.067 grm. of milk-sugar; or its amount may be estimated by means of the saccharimeter (§ 150). **Proteids** are precipitated and the fats extracted with ether. The fats in fresh milk form about 3 per cent., and in skimmed milk $1\frac{1}{2}$ per cent. The amount of water in relation to the milk-globules is estimated by the **lactoscope** or the **diaphanometer** of Donné (modified by Vogel and Hoppe-Seyler), which consists of a glass vessel with plane parallel sides placed 1 centimetre apart. A measured quantity of milk is taken, and water is added to it from a burette until the outline of a candle flame placed at a distance of 1 metre can be distinctly seen through the diluted milk. This is done in a dark room. For 1 cubic centimetre of good cow's milk, 70 to 85 centimetres water are required. [Other forms of lactoscope are used, all depend-

ing on the same principle of an optical test, viz., that the opacity of milk varies with and is proportional to the amount of butter-fats present, *i.e.*, the oil-globules. Bond uses a shallow cylindrical vessel with the bottom covered by black lines on a white surface. A measured quantity of water is placed in this vessel, and milk is added drop by drop, until the parallel lines on the pattern at the bottom of the dish cease to be visible. On counting the number of drops a table accompanying the appliance gives the percentage of fats. This method gives approximate results. In all cases it is well to use fresh milk.]

Various substances pass into the milk when they are administered to the mother—many odorous vegetable bodies, *e.g.*, anise, vermouth, garlic, &c.; chloral, rhubarb, opium, indigo, salicylic acid, iodine, iron, zinc, mercury, lead, bismuth, antimony. In osteomalacia the amount of lime in the milk is increased (*Gusserow*). Potassium iodide diminishes the secretion of milk by affecting the secretory function. Amongst **abnormal constituents** are—hæmoglobin, bile-pigments, mucus, blood-corpuscles, pus, fibrin. Numerous fungi and other low organisms develop in evacuated milk, and the rare *blue* milk is due to the development of *Bacillus cyanogenus*. The milk-serum is blue, not the fungus. Blue milk is unhealthy, and causes diarrhoea. There are fungi which make milk *bluish-black* or *green*. *Red* and *yellow* milk are produced by a similar action of chromogenic fungi (§ 184). The former is produced by *Micrococcus prodigiosus*, which is colourless. The colour seems to be due to fuchsin. The yellow colour is produced by *Bacillus synxanthus*. Some of the pigments seem to be related to the aniline-, and others to the phenol-colouring matters (*Hüppe*).

The **rennet-like action of bacteria** is a widely diffused property of these organisms; they coagulate and peptonise casein, and may ultimately produce further decompositions. The butyric acid bacillus (§ 184) first coagulates casein, then peptonises it, and finally splits it up, with the evolution of ammonia (*Hüppe*).

Milk becomes *stringy* owing to the action of cocci which form a stringy substance [= *dextran*, $C_{12}H_{10}O_{10}$ (*Scheibler*)], just as beer or wine undergoes a similar or ropy change. [The milk of diseased animals may contain or transmit directly infectious matter.]

Preparations of Milk.—(1) **Condensed Milk.**—80 grms. cane-sugar are added to 1 litre of milk; the whole is evaporated to $\frac{1}{2}$; and while hot sealed up in tin cans. For children one teaspoonful is dissolved in a pint of cold water, and then boiled.

(2) **Koumiss** is prepared by the Tartars from mare's milk. After the addition of koumiss and sour milk, the whole is violently stirred, and it undergoes the alcoholic fermentation, whereby the milk-sugar is first changed into galactose, and then into alcohol; so that koumiss contains 2 to 3 per cent. of alcohol; while the casein is at first precipitated, but is afterwards partly redissolved and changed into acid-albumin and peptone. Tartar koumiss seems to be produced by the action of a special bacterium (*Diaspora caucasia*).

[**How is Milk formed?**—It is obvious from its chemical composition that milk is not a simple transudation from the blood, for casein and lactose occur in it in large amount, and neither of these is present in the blood; moreover, there is much fat, which occurs only in small amount in the blood. Lastly, the ash of milk is quantitatively different from the ash of blood-plasma. Milk, therefore, is a chemical product, due to the secretory activity of the cells of the mammary glands, which find only the raw material in the blood, and from this, by their own subtle chemistry, manufacture the specific products of the milk.]

[**Source of the Fats.**—A plentiful supply of **proteid** food increases the amount of milk and its specific constituents, but most of all it increases its richness in fats. It seems clear that the fats of milk are not derived from the fats taken with the food, but are obtained from the splitting up of proteid molecules, and we know that albumin does split up under certain conditions into a nitrogenous and a non-nitrogenous molecule. Further, in a bitch fed on pure flesh diet, the milk contains a very large amount of fat.]

[The addition of fat to the food rather diminishes than increases the fats of the milk, if there be not simultaneously sufficient proteids in the food.]

[**Source of the Sugar.**—The carbohydrates of the food have no effect on the amount of sugar in the milk, and even in herbivora there is no special effect to be noted. The greatest part of the sugar is also derived from the proteids, for bitches fed on an exclusively animal diet (flesh) yield a considerable amount of sugar.]

[**Source of Casein.**—This seems to be derived from the proteids of the blood and lymph.]

[To increase the quantity of milk, therefore, proteid food must be given.]

[**Margarine or artificial butter.**—The best form is beef fat freed from its stearin and mixed with milk or genuine butter-colouring and flavouring ingredients. If prepared from wholesome pure animal fats, it has a nutritive value little inferior to butter, but it seems to be less assimilable than butter.]

(3) **Cheese** is prepared by coagulating milk with rennet, allowing the whey to separate, and adding salt to the curd. When kept for a long time cheese "**ripens**," the casein again becomes soluble in water, probably from the formation of soda albuminate; in many cases it becomes semi-fluid, when it takes the characters of peptones. When further decomposition occurs, leucin and tyrosin are formed. [The word tyrosin is derived from *Τυρός*, cheese.] The fats increase at the expense of the casein, and they again undergo further change, the volatile fatty acids giving the characteristic odour.

The formation of peptone, leucin, tyrosin, and the decomposition of fat recall the digestive processes. [Cheese is coagulated casein, entangling more or less fat, so that the richness of the cheese will depend upon the kind of milk from which it is made. There are, in this sense, three kinds of cheese, *whole milk*, *skim milk*, and *cream cheese*, the last being represented by Stilton, Roquefort, Cheshire, &c. The composition is shown in the following table after Bauer :—

	Water.	Nitrogenous Matter.	Fat.	Extractives.	Ash.
Cream cheese, .	35.75	7.16	30.43	2.53	4.13
Whole milk, . .	46.82	27.62	20.54	2.97	3.05
Skim milk, . .	48.02	32.65	8.41	6.80	4.12

Cream cheese, especially if it be made from the goat's milk, acquires a very high odour and strong flavour when it is kept and "**ripens**"; the casein is partly decomposed to yield ammonia and ammonium sulphide, while the fats yield butyric, caproic, and other acids.]

232. EGGS must be regarded as a complete food, as the organism of the young chick is developed from them. The **yolk** contains a characteristic proteid body—*vitellin* (§ 249), and an *albuminate* in the envelopes of the yellow yolk spheres—*nuclein*, from the white yolk; *fats* in the yellow yolk (palmitin, olein), cholesterolin, much *lecithin*, and as its decomposition-product, glycerin-phosphoric acid; *grape-sugar*, *pigments* (lutein), and a body containing iron and related to hæmoglobin; lastly, *salts* qualitatively the same as in blood—quantitatively as in the *blood-corpuscles*—and *gases*. The chief constituent of the **white of egg** is *egg-albumin* (§ 249), together with a small amount of palmitin and olein partly saponified with soda; grape-sugar, extractives; lastly salts, qualitatively resembling those of blood, but quantitatively like those of *serum*, and a trace of fluorine. Relatively more of the nitrogenous constituents than of the fatty constituents of eggs are absorbed (*Rubner*). [Considered as a food, eggs are obviously deficient in carbohydrates.]

[The **shell** is composed chiefly of mineral matter (91 per cent. of calcic carbonate, 6 per cent. of calcic phosphate, and 3 per cent. of organic matter). A hen's egg weighs about $1\frac{3}{4}$ oz., of which the shell forms about $\frac{1}{10}$. Note the amount of fats in the yolk.]

Composition :—

	White of Egg. Yolk.			White of Egg. Yolk.	
Water, . . .	84.8	51.5	Mineral matter, .	1.2	1.4
Proteids, . .	12.0	15.0	Pigment extractives, . . .	...	2.1
Fats, &c., . .	2.0	30.0			

233. FLESH AND ITS PREPARATIONS.—Flesh, in the form in which it is eaten, contains, in addition to the muscle-substance proper, more or less of the elements of fat, connective- and elastic-tissue mixed with it (§ 293). The following results refer to flesh freed as much as possible from those constituents. The chief

proteid constituent of the contractile muscular substance is **myosin**; *serum-albumin* occurs in the fluid of the fibres, in the lymph and blood of muscle. The *fats* are for the most part derived from the interfascicular fat-cells, while *lecithin* and *cholesterin* come from the nerves of the muscles; the *gelatin* is derived from the connective-tissue of the perimysium, perineurium, and the walls of blood-vessels and tendons. The *red colour* of the flesh is due to the hæmoglobin present in the sarcoous substance, but in some muscles, *e.g.*, the heart, there is a special pigment, myohæmatin (*MacMunn*), [although the latter statement is denied by Hoppe-Seyler.] *Elastin* occurs in the sarcolemma, neurilemma, and in the elastic fibres of the perimysium and walls of the vessels; the small amount of *keratin* is derived from the endothelium of the vessels. The chief muscular substance, the result of the retrogressive metabolism of the sarcoous substance, is *kreatin* (-0.05 per cent.); *kreatinin*, sometimes *inosinic acid*, then lactic, or rather *sarcolactic acid* (§ 293). Further, *taurin*, *sarkin*, *xanthin*, *uric acid*, *carnin*, *inosit* (most abundant in the muscles of drunkards), *urea* (0.1 per cent. [but in the dog-fish 1.95 per cent.]), *dextrin* (in horse and rabbit, not constant); *grape-sugar*, but this is very probably derived *post-mortem* from glycogen (0.43 per cent.), which occurs in considerable amount in foetal muscles; lastly, volatile *fatty acids*. Amongst the **salts**, potash and phosphoric acid compounds are most abundant; magnesium phosphate exceeds calcium phosphate in amount. [The composition varies somewhat even in different muscles of the same animal.]

In 100 parts **Flesh** there are, according to Schlossberger and v. Bibra—

	Ox.	Calf.	Deer.	Pig.	Man.	Fowl.	Carp.	Frog.
Water, ...	77.50	78.20	74.63	78.30	74.45	77.30	79.78	80.43
Solids, ...	22.50	21.80	25.37	21.70	25.55	22.7	20.22	19.57
Soluble albumin, ...	2.20	2.60	1.94	2.40	1.93	3.0	2.35	1.86
Colouring matter, ...								
Glutin, ...	1.30	1.60	0.50	0.80	2.07	1.2	1.98	2.48
Alcoholic extract, ...	1.50	1.40	4.75	1.70	3.71	1.4	3.47	3.46
Fats, ...	...	...	1.30	...	2.30	...	1.11	0.10
Insoluble albumin, ...								
Blood-vessels, &c., ...	17.50	16.2	16.81	16.81	15.54	16.5	11.31	11.67

In 100 parts **Ash** there are —

	Horse.	Ox.	Calf.	Pig.
Potash, ...	39.40	35.94	34.40	37.79
Soda, ...	4.86	...	2.35	4.02
Magnesia, ...	3.88	3.31	1.45	4.81
Chalk, ...	1.80	1.73	1.99	7.54
Potassium, ...	...	5.36	...	...
Sodium, ...	1.47	4.86	10.59	0.40
Chlorine, ...				
Iron oxide, ...	1.0	0.98	0.27	0.35
Phosphoric Acid, ...	46.74	34.36	48.13	44.47
Sulphuric, ...	0.30	3.37	...	...
Silicic, ...	...	2.07	0.81	...
Carbonic, ...	...	8.02	...	...
Ammonia, ...	...	0.15	...	...

The amount of fat in flesh varies very much according to the condition of the animal. After removal of the visible fat, human flesh contains 7.15 ; ox, 11.12 ; calf, 10.4 ; sheep, 3.9 ; wild goose, 8.8 ; fowl, 2.5 per cent.

The amount of **extractives** is most abundant in those animals which exhibit energetic

muscular action ; hence it is largest in wild animals. The extract is increased after vigorous muscular action, whereby sarcolactic acid is developed, and the flesh becomes more tender and is more palatable. Some of the extractives excite the nervous system, *e.g.*, kreatin and kreatinin ; and others give to flesh its characteristic agreeable flavour ["osmasome,"] but this is also partly due to the different fats of the flesh, and is best developed when the flesh is cooked. The extractives in 100 parts of flesh are in man and pigeon, 3 ; deer and duck, 4 ; swallow, 7 per cent.

[Flesh is characterised by its large percentage of proteids containing four times as much as milk. The flesh of birds contains most proteids, then follows that of mammals, and then fishes.]

[Munk gives the following table of its composition—

In 100 Parts Flesh.	Ox.	Calf.	Pig.	Horse.	Fowl.	Pike.
Water, ...	76·7	75·6	72·6	74·3	70·8	79·3
Solids, ...	23·3	24·4	27·4	25·7	29·2	20·7
Myosin, albumin, and gelatin, ... }	20·0	19·4	19·9	21·7	22·7	18·3
Fat, ...	1·5	2·9	6·2	2·5	4·1	0·7
Carbohydrates, . . .	0·6	0·8	0·6	0·6	1·3	0·9
Salts, ...	1·2	1·3	1·1	1·0	1·1	0·8]

Cooking of Flesh.—As a general rule, the flesh of *young* animals, owing to the sarcolemma, connective-tissue, and elastic constituents being less tough, is more tender and more easily digested than the flesh of old animals ; after flesh has been kept for a time it is more friable and tender, as the inosit becomes changed into sarcolactic acid and the glycogen into sugar, and this again into lactic acid, whereby the elements of the flesh undergo a kind of maceration. Finely divided flesh is more digestible than when it is eaten in large pieces. In cooking meat, the heat ought not to be too intense, and ought not to be continued too long, as the musenlar fibres thereby become hard and shrink very much. Those parts are most digestible which are obtained from the centre of a roast where they have been heated to 60° to 70° C., as this temperature is sufficient, with the aid of the acids of the flesh, to change the connective-tissue into gelatin, whereby the fibres are loosened, so that the gastric juice readily attacks them. In roasting beef, apply heat suddenly at first, to coagulate a layer on the surface, which prevents the escape of the juice.

Meat Soup is best prepared by cutting the flesh into pieces and placing them for several hours in cold water, and afterwards boiling. Liebig found that 6 parts per 100 of ox flesh were dissolved by cold water. When this cold extract was boiled, 2·95 parts were precipitated as coagulated albumin, which is chiefly removed by "skimming," so that only 3·05 parts remain in solution. From 100 parts of flesh of fowl, 8 parts were extracted, and of these 4·7 was coagulated and 3·3 remained dissolved in the soup. By boiling for a very long time, part of the albumin may be redissolved. The dissolved substances are :—(1) Inorganic salts of the meat, of which 82·27 per cent. pass into the soup ; the earthy phosphates chiefly remain in the cooked meat. (2) Kreatin, kreatinin, the inosinates and laetates which give to broth or beef-tea their stimulating qualities, and a small amount of aromatic extractives. (3) Gelatin, more abundantly extracted from the flesh of young animals. According to these facts, therefore, flesh broth or beef-tea is a powerful stimulant, supplying muscle with restoratives, but is not a food in the ordinary sense of the term, as kreatin in general leaves the body unchanged (*v. Voit*). The flesh, especially if it be cooked in a large mass, after the extraction of the broth, is still available as a food.

Liebig's Extract of Meat is an extract of flesh evaporated to a thick syrupy consistence. It contains no fat or gelatin or proteid, and is chiefly a solution of the extractives and salts of flesh. [It contains about 22 per cent. of water and 78 of solids. Of the latter—which contain no proteids—61 per cent. is organic, and 17 inorganic salts. Crystals of kreatin are found in large numbers in the extract.]

Extract of Fish.—A similar extract is now prepared from fish ; and such extract has no fishy flavour, but presents much the same appearance, odour, and properties as extract of flesh.]

Beef-Tea made by putting the meat, cut up into small pieces, in cold water and then gradually heating it, is really a watery extract of certain of the constituents of meat. It has slight nutritive and stimulating properties, and may be regarded as a watery solution of the extractives, and salts of meat together with gelatin, minute quantities of soluble albumin, and, perhaps, some fat floating on the surface of the fluid.]

Preservation of Meat.—Much "preserved" meat in tins is now used. The Indians dry strips of meat in the sun's rays to form pemmican. "Pickling" or salting meat is much practised. Voit

found that where meat is placed in brine its nutritive value is not greatly impaired. In salted meat, besides an increase of salt, he found a loss of 10·4 per cent. of water and of organic matters 2·1, albumin 1·1, extractives 13·5, and phosphoric acid 8·5 per cent. When meat is “smoked” the surface becomes harder, and the meat is acted on by creosote and other antiseptics present in the smoke of the wood used in the process.]

234. VEGETABLE FOODS.—The nitrogenous constituents of plants are not so easily absorbed as animal food (*Rubner*). Still if they contain the same amount of N they may completely replace animal proteids (*Rutgers*), [and, according to Hoppe-Seyler, the vegetable proteids do not seem to differ essentially from animal proteids.] Carbohydrates, starch, and sugar are very completely absorbed, and even a not inconsiderable proportion of cellulose may be digested (§ 184, I). The more fats that are contained in the vegetable food, the less are the carbohydrates digested and absorbed.

[Vegetable foods are characterised by the very large amount of non-nitrogenous substance they contain, and by the fact that this is usually contained in cellulose capsules, which are either not or with difficulty dissolved by the digestive juices, and they always yield a considerable amount of indigestible residue, so that the herbivorous animals always pass a larger quantity of fæces than carnivorous. Moreover, vegetable food is not so fully utilised in the digestive tract as animal food (p. 435). Further, the potash and magnesia, especially the phosphatic salts, are more abundant than soda and lime, while there is little chlorine (*Munk*).]

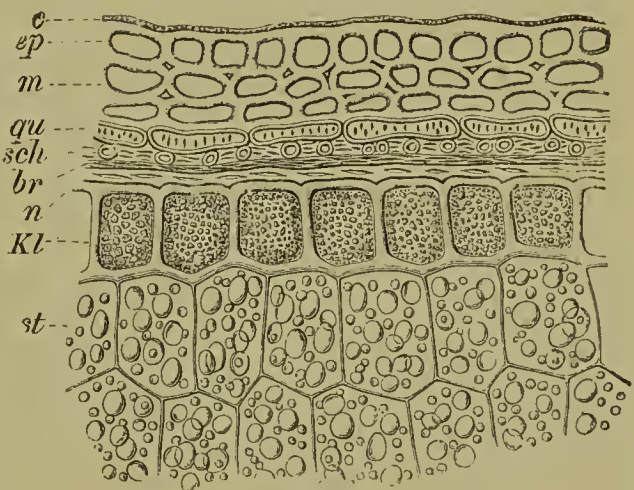


Fig. 290.

1. The **cereals** are most important vegetable foods; they contain proteids, starch, salts, and about 14 per cent. of water. The nitrogenous body **glutin** is most abundant under the husk (fig. 290, *Kl*). The use of whole meal containing the outer layers of the grain is highly nutritive, but bread containing much bran is somewhat indigestible (*Rubner*). Their composition is the following:—

100 Parts of the Dry Meal contain			100 Parts of Ash contain		
Of	Albumin.	Starch.	Red Wheat.		White Wheat.
Wheat,	16·52%	56·25%	27·87	Potash,	33·84
Rye,	11·92	60·91	15·75	Soda,	...
Barley,	17·70	38·31	1·93	Lime,	3·09
Maize,	13·65	77·74	9·60	Magnesia,	13·54
Rice,	7·40	86·21	1·36	Iron oxide,	0·31
Buckwheat,	6·8-10·5	65·05	49·36	Phosphoric Acid,	59·21
			0·15	Silica,	...

It is curious to observe that soda is absent from white wheat, its place being taken by other alkalies. Rye contains more cellulose and dextrin than wheat, but less sugar; rye-bread is usually less porous.

The following table by König gives their composition although they vary much with climate, soil, cultivation, &c.

In 100 Parts.	Wheat.	Rye.	Barley.	Oats.	Rice.	Maize.
Water, ...	13.6	11.1	13.8	12.4	13.1	13.1
Proteid, ...	12.4	11.5	11.1	10.4	7.9	9.9
Fat, ...	1.8	1.8	2.2	5.2	0.9	4.6
Carbohydrates and N-free extractives,	67.9	67.8	64.9	57.8	76.5	68.4
Cellulose, ...	2.5	2.0	5.3	11.2	0.6	2.5
Ash, ...	1.8	1.8	2.7	3.0	1.0	1.5

The cereals have an outer envelope composed of **cellulose** : to facilitate digestion of the contents the cellulose envelopes are crushed or removed by the process of "milling ;" the finely ground contents constitute flour or meal.

[**Oatmeal** contains more nitrogenous substances (gliadin and gluten-casein) than wheaten flour, but owing to the want of adhesive properties it cannot be made into bread. The amount of fat and salts is large (p. 436).]

In the preparation of bread the meal is kneaded with water until dough is formed, and to it is added salt and *yeast* (*Saccharomyces cerevisie*). When placed in a warm oven, the proteids of the meal begin to decompose and act as a ferment upon the swollen-up starch, which becomes in part changed into sugar. The sugar is further decomposed into CO₂ and alcohol, the CO₂ forms bubbles, which cause the bread to "rise," and thus become spongy and porous. The alcohol is driven off by the baking (200°), while much soluble dextrin is formed in the crust of the bread. [But CO₂ may be set free within the dough by chemical means without yeast or leaven, thus forming **unfermented bread**. This is done by mixing with the dough an alkaline carbonate, and then adding an acid. Baking powders consist of carbonate of soda and tartaric acid. In Darglish's process for **aerated** bread, the CO₂ is forced into water, and a dough is made with this water under pressure, and when the dough is heated, the CO₂ expands and forms the spongy bread. Bread as an article of food is deficient in N, while it is poor in fats and some salts. Hence the necessity for using some form of fat with it (butter or bacon).]

2. The **leguminous seeds** or **pulses** contain much **proteid**, *especially legumin* ; together with starch, lecithin, cholesterin, and 9 to 19 per cent. water. Owing to the absence of gluten, they do not form dough, and bread cannot be prepared from them. On account of the large amount of proteids which they contain, and on account of their cheapness, they are admirably adapted as food for the poorer classes ; excellent soup can be made with them.

[The following table from Munk shows their composition contrasted with that of potatoes :—

In 100 Parts.	Lentils.	Peas.	Beans.	Potatoes.
Water, ...	12.5	14.3	14.8	76.0
Proteids, ...	24.8	22.6	23.7	2.0
Fat, ...	1.9	1.7	1.6	0.2
Carbohydrates, ...	54.8	53.2	49.3	20.6
Cellulose, ...	3.6	5.5	7.5	0.7
Ash, ...	2.4	2.7	3.1	1.0

[3. The whole group of **farinaceous substances** used as "**pudding stuffs**," such as corn-flour, arrow-root, rice, hominy, are really very largely composed of starchy substances.]

4. **Potatoes** contain 70 to 81 per cent. water, and of the solids about 20 per cent. consists of starch. In the fresh juicy cellular tissue, which has an acid reaction, from the presence of phosphoric, malic, and hydrochloric acids, there is 16 to 23 per cent. of starch, 2.5 soluble albumin, globulin, and a trace of asparagin. The

envelopes of the cells swell up by boiling, and are changed into sugar and gums by dilute acids. The cells contain a large number of starch granules (fig. 291). The poisonous solanin occurs in the sprouts. In 100 parts of *potato ash*, May found 49·96 potash, 2·41 sodium chloride, 8·11 potassium chloride, 6·50 sulphuric acid derived from burned proteids, 7·17 silica.

5. In **fruits** the chief nutrient ingredients are sugar and salts; the organic acids give them their characteristic taste, the gelatinising substance is the soluble so-called **pectin** ($C_{32}H_{48}O_{32}$), which can be prepared artificially by boiling the very insoluble pectose of unripe fruits and mulberries.

6. **Green Vegetables** are especially rich in salts, which resemble the salts of the blood; thus, dry salad contains 23 per cent. of salts, which closely resemble the salts of the blood. Of much less importance are the starch, cell-substance, dextrin, sugar, and the small amount of albumin which they contain.

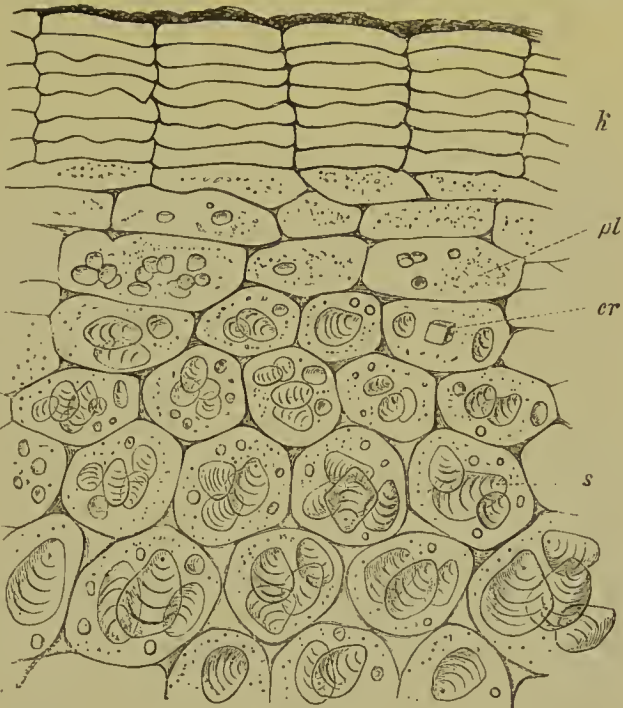


Fig. 291.

Section of part of a potato. *K*, capsule; *pl*, plasma containing cells with small starch-grains; *r*, protein crystals; *s*, starch.

[Vegetables are chiefly useful for the salts they contain, while many of them are **antiscorbutic**. Their value is attested by the serious defects of nutrition, such as scurvy, which result when they are not supplied in the food. In Arctic expeditions and the navy, lime juice is served out as an antiscorbutic.]

[**Salts of Vegetable Food.**—Much interest attaches to the large amount of **potash** salts in vegetable food. They contain 2–8 times as much potash as soda, so that herbivora take 5–10 times as much potash as soda in their food. Bunge has shown that this large consumption of potash salts by certain of these animals is the cause of the great amount of common salt required by them (*Munk*).]

[**Preserved Vegetables.**—The dried and compressed vegetables of Messrs Chollet & Company are an excellent substitute for fresh vegetables, and are used largely in naval and military expeditions.]

[**Utilisation of Food.**—As regards what percentage of the food swallowed is actually absorbed, we know that, stated broadly, vegetable food is assimilated to a much less extent than animal food in man. Fr. Hofmann gives the following table as showing this:—

Weight of Food.	Vegetable.		Animal.	
	Digested.	Undigested.	Digested.	Undigested.
Of 100 parts of solids, ...	75·5	24·5	89·9	11·1
„ 100 „ albumin, ...	46·6	53·4	81·2	18·8
„ 100 „ fats or carbohydrates, ...	90·3	9·7	96·9	3·1]

[The following table, abridged from Parkes, shows the composition of the chief articles of diet, and is also used for calculating diet tables :—

Articles.	Water.	Proteids.	Fats.	Carbo- hydrates.	Salts.
Beef Steak, ...	74.4	20.5	3.5	...	1.6
Fat pork, ...	39.0	9.8	48.9	...	2.3
Smoked ham, ...	27.8	24.0	36.5	...	10.1
White fish, ...	78.0	18.1	2.9	...	1.0
Poultry, ...	74.0	21.0	3.8	...	1.2
White wheaten bread, ...	40.0	8.0	1.5	49.2	1.3
Wheat flour, ...	15.0	11.0	2.0	70.3	1.7
Biscuit, ...	8.0	15.6	1.3	73.4	1.7
Rice, ...	10.0	5.0	0.8	83.2	0.5
Oatmeal, ...	15.0	12.6	5.6	63.0	3.0
Maize, ...	13.5	10.0	6.7	64.5	1.4
Macaroni, ...	13.1	9.0	0.3	76.8	0.8
Arrow-root, ...	15.4	0.8	...	83.3	0.27
Peas (dry), ...	15.0	22.0	2.0	53.0	2.4
Potatoes, ...	74.0	2.0	0.16	21.0	1.0
Carrots, ...	85.0	1.6	0.25	8.4	1.0
Cabbage, ...	91.0	1.8	5.0	5.8	0.7
Butter, ...	6.0	0.3	91.0	...	2.7
Egg ($\frac{1}{10}$ for shell), ...	73.5	13.5	11.6	...	1.0
Cheese, ...	36.8	33.5	24.3	...	5.4
Milk (S. G. 1032), ...	86.8	4.0	3.7	4.8	0.7
Cream, ...	66.0	2.7	26.7	2.8	1.8
Skimmed milk, ...	88.0	4.0	1.8	5.4	0.8
Sugar, ...	3.0	..	...	96.5	0.5]

235. CONDIMENTS, COFFEE, TEA, ALCOHOL.—Some substances are used along with food, not so much on account of their nutritive properties as on account of their stimulating effects and agreeable qualities, which are exerted partly upon the organ of taste and partly upon the nervous system. These are called **condiments**.

Coffee, Tea, and Chocolate are prepared as infusions of certain vegetables [the first of the roasted berry the second of the leaves, and the third of the seeds]. Their chief active ingredients are respectively **caffein**, **thein** ($C_8H_{10}N_4O_2 + H_2O$ trimethylxanthin), and **theobromin** ($C_7H_8N_4O_2$ dimethylxanthin), which are regarded as alkaloids of the vegetable bases, and which have recently been prepared artificially from xanthin (*E. Fischer*). [**Guarana**, or Brazilian cocoa, is made of the seeds ground into a paste in the form of a sausage. **Maté** or Paraguay tea (the leaves of a species of holly) is used in South America, and so also is the **coca** of the Andes (*Erythroxylon Coca*).] These "**alkaloids**" occur as such in the plants containing them; they behave like ammonia; they have an alkaline reaction, and form crystalline salts with acids. All these vegetable bases act upon the nervous system; some more feebly (as the above), others more powerfully (quinine); some stimulate powerfully, or completely paralyse (morphia, atropin, strychnin, eurarin, nicotin).

Effects of Tea and Coffee.—All these substances act on the nervous system; they quicken thought, accelerate movement, and stir one to greater activity. In these respects they resemble the stimulating extractives of beef-tea. Coffee contains about $\frac{1}{3}$ per cent. of caffein, part of which only is liberated by the act of roasting. Tea has 6 per cent. of thein; whilst green tea contains 1 per cent. ethereal oil, and black tea $\frac{1}{2}$ per cent.; in green tea there is 18 per cent., in black 15 per cent. tannin; green tea yields about 46 per cent., and the black scarcely 30 per cent. of extract. The **inorganic salts** present are also of importance; tea contains 3.03 per cent. of salts, and amongst these are soluble compounds of iron, manganese, and soda-salts. In coffee, which yields 3.41 per cent. of ash, potash salts are most abundant; in all three substances the other salts which occur in the blood are also present.

Alcoholic drinks owe their action chiefly to the alcohol which they contain. Alcohol, when taken into the body, undergoes certain changes and produces certain

effects—(1) About 95 per cent. of it is oxidised chiefly into CO_2 and H_2O , so that it is so far a source of heat. As it undergoes this change very readily, when taken to a certain extent, it may act as a substitute for the consumption of the tissues of the body, especially when the amount of food is insufficient. [Hammond found that when he lived on an insufficient amount of food, alcohol, if given in a certain quantity, supplied the place of the deficiency of food, and he even gained in weight. If, however, sufficient food was taken, alcohol was unnecessary. As it interferes with oxidation, and where there is a sufficient amount of other food, in health it is unnecessary for dietetic purposes.] Small doses diminish the decomposition of the proteids to the extent of 6 to 7 per cent. Only a very small part of the alcohol is excreted in the urine; the odour of the breath is not due to alcohol, but to other volatile substances mixed with it, *e.g.*, fusel oil, &c. (2) In small doses it excites, while in large doses it paralyses the nervous system. By its stimulating qualities it excites to greater action, which, however, is followed by depression. (3) It diminishes the sensation of hunger. (4) It excites the vascular system, accelerates the circulation, so that the muscles and nerves are more active, owing to the greater supply of blood. It also gives rise to a subjective feeling of warmth. In large doses, however, it paralyses the vessels, so that they dilate, and thus much heat is given off (§ 213, 7; § 227) and the temperature is lowered. The action of the heart also becomes affected, the pulse becomes smaller, feebler, and more rapid. In high altitudes the action of alcohol is greatly lessened, owing to the diminished atmospheric pressure, whereby it is rapidly given off from the blood.

Alcohol in small doses is of great use in conditions of **temporary want**, and where the food taken is insufficient in quantity. When alcohol is taken regularly, more especially in large doses, it affects the nervous system, and undermines the psychical and corporeal faculties, partly from the action of the impurities which it may contain, such as fusel oil, which has a poisonous effect upon the nervous system, partly by the direct effects, such as catarrh and inflammation of the digestive organs, which it produces, and lastly, by its effect upon the normal metabolism.

[The action of alcohol in **lowering the temperature**, even in moderate doses, is most important. By dilating the cutaneous vessels, it thus permits of the radiating of much heat from the blood. When the action of alcohol is pushed too far, and especially when this is combined with the action of great cold, its use is to be condemned. Brunton has pointed out that, as regards its action on the **nervous system**, it seems to induce progressive paralysis, affecting the nervous tissues "in the inverse order of their development, the highest centres being affected first and the lowest last." The *judgment* is affected first, although the imagination and "emotions may be more than usually active." The *motor centres* and *speech* are affected, then the cerebellum is influenced, and afterwards the cord, while by and by the centres essential to life are paralysed, provided the dose be sufficiently large.]

Preparation.—Alcoholic drinks are prepared by the **fermentation** of various carbohydrates, such as sugar derived from starch. The alcoholic fermentation, such as occurs in the manufacture of beer, is caused

by the development of the yeast plant, *Saccharomyces cerevisiæ*; while in the fermentation of the grape (wine), *S. ellipsoideus* is the species present (fig. 292). The yeast takes the substances necessary



Fig. 292.

1, Isolated yeast cells; 2, 3, yeast cells budding; 4, 5, so-called endogenous formation of cells; 6, sprouting and formation of buds.

for the maintenance of its organic processes directly from the mixture of the sugar, *viz.*, carbohydrates, proteids, and salts, especially calcium and potassium phosphates and magnesium sulphate. These substances undergo decomposition within the cells of the yeast plant, which multiply during the process, and there are produced alcohol and CO_2 (§ 150), together with glycerin (3.2 to 3.6 per cent.) and succinic acid (0.6 to 0.7 per cent.). Yeast is either added intentionally or it reaches the mixture from the air, which always contains its spores. When yeast is completely excluded, or if it be killed by boiling [or if its action be

prevented by the presence of some germicide], the fermentation does not occur. The alcoholic fermentation is due to the vital activity of a low organism.

In the preparation of **brandy**, the starch of the grain or potatoes is first changed into sugar by the action of diastase or maltin. Yeast is added, and fermentation thereby produced; the mixture is distilled at 78.3°C . The fusel oil is prevented from mixing with the alcohol by passing the vapour through heated charcoal. The distillate contains 50 to 55 per cent. of alcohol.

In the preparation of **wine**, the saccharine juice of the grape—the **must**—after being expressed from the grapes, is exposed to the air at 10° to 15°C ., and the yeast cells, which are floating about, drop into it and excite fermentation, which lasts 10 to 14 days, when the yeast sinks to the bottom. The clear wine is drawn off into casks, where it becomes turbid by undergoing an after-fermentation, until the sugar is converted into alcohol and CO_2 , which is accompanied by the deposition of some yeast and tartar. If all the sugar is not decomposed—which occurs when there is not sufficient nitrogenous matter present to nourish the yeast—a *sweet wine* is obtained. Wine contains 89 to 90 per cent. water, 7 to 8 per cent. alcohol, consisting of ethylic, propylic, and butylic alcohols. The red colour of some wines is due to the colouring matter of the skin of the grapes, but if the skins be removed before fermentation, red grapes yield white wine. When wine is stored, it develops a fine flavour or bouquet. The characteristic vinous odour is due to **œnanthic ether**. The *salts* of wine closely resemble the salts of the blood.

In the preparation of **beer** the grain is moistened, and allowed to germinate, when the temperature rises, and the starch (68 per cent. in barley) is changed into sugar. Thus "**malt**" is formed, which is dried, and afterwards pulverised, and extracted with water at 70° to 75° , the watery extract being the "**wort**." Hops are added to wort, and the whole is evaporated, when the proteids are coagulated. Hops give beer its bitter taste, and make it keep, while their tannic acid precipitates any starch that may be present, and clarifies the wort. After being boiled, it is cooled rapidly (12°C .); yeast is added, and fermentation goes on rapidly and with considerable effervescence at 10° to 14° . Beer contains 75 to 95 per cent. water; alcohol, 2 to 5 per cent. (porter and ale, to 8 per cent.); CO_2 , 0.1 to 0.8 per cent.; sugar, 2 to 8 per cent.; gum, dextrin, 2 to 10 per cent.; the hops yield traces of protein, fat, lactic acid, ammonia compounds, the salts of the grain and of the hops. In the **ash** there is a great preponderance of phosphoric acid and potash, both of which are of great importance for the formation of blood. In 100 parts of ash there are 40.8 potash, 20.0 phosphorus, magnesium phosphate 20, calcium phosphate 2.6, silica 16.6 per cent. The formation of blood, muscle, and other tissues from the consumption of beer is due to the phosphoric acid and potash, while if too much be taken, the potash produces fatigue.

Condiments are taken with food, partly on account of their taste, and partly because they excite secretion. Common salt, in a certain sense, is a condiment. We may also include as such many substances of unknown constitution which act upon the gustatory organs, *e.g.*, dextrin, and substances in the crust of bread and in meat which has been roasted.

236. EQUILIBRIUM OF THE METABOLISM.—By this term is meant that, under normal physiological conditions, just as much material is absorbed and assimilated from the food as is removed from the body by the excretory organs in the form of effete or end-products, the result of the retrogressive tissue-changes. The income must always balance the expenditure; wherever a tissue is used up, it must be replaced by the formation of new tissue. During the period of **growth**, the increase of the body corresponds to an increased formative activity whereby the metabolism of the growing parts of the body is 2.5 to 6.3 times greater than that of the parts already formed. Conversely, during senile **decay**, there is an excess of expenditure from the body.

Methods.—The normal equilibrium of the metabolism of the body is investigated—(1) By determining chemically that the sum of all the substances passing into the body is equal to the sum of all the substances given off from it. Thus the C, N, H, O, salts and water of the food, and the O inspired, must be equal to the C, N, H, O, salts and water given off in the excreta (urine, faeces, air expired, water excreted). (2) The **physiological equilibrium** is determined empirically by observing that the body retains its normal weight with a given diet; so that, by simply weighing a person, a physician is enabled to determine exactly the state of convalescence of his patient. The tedious process of making an **elementary analysis** of the metabolic substances was first undertaken in the Munich School by v. Bischoff, v. Voit, v. Pettenkofer, and others.

Circulation of C.—In the circulation of materials the total amount of **C** taken in

the food, if the metabolism be in a condition of physiological equilibrium, must be equalled by the C in the CO_2 given off by the lungs and skin (90 per cent.), together with the relatively small amount of C in the organic excreta of the urine and fæces (10 per cent.).

Circulation of N.—*Nearly all the N* taken in with the food is excreted within twenty-four hours in the form of urea. A very small amount of nitrogenous matter is excreted in the fæces, while the other nitrogenous urinary constituents (uric acid, kreatinin, &c.) represent about 2 per cent. of N. A trace of the N is given off by the breath (§ 124), and a minute proportion in combination, in the epidermal scales (50 milligrams daily in the hair and nails), and in the sweat.

Deficit of N.—That nearly all the N taken in the food reappears in the urine and fæces, as was stated by v. Voit to be the case in the carnivora and in the herbivora, and by v. Ranke in man, is contradicted partly by old and partly by new observations, which go to show that the whole of the N cannot be recovered from these excretions, but that on the contrary there is a *deficit*.

According to Leo, only 0.55 per cent. of the albumin transformed within the body (assuming 15 per cent. N in albumin) gives off its N in the form of gaseous N (according to Seegen and Nowak 12 times more). In every exact analysis of the metabolism of N this gaseous excretion of N must be taken into account.

The excretion of N after food does not take place regularly from hour to hour, but it increases at once and distinctly, reaches its maximum in five to six hours, and then gradually falls. The same is true of the excretion of S and P; but in these cases the maximum of excretion is reached at the fourth hour. When fat is added to a diet of flesh, the excretion of N and S is uniformly distributed over the individual hours of the day (*v. Voit and Feder*).

The nitrogenous constituents in the body during metabolism become poorer in C, and richer in N and O. Thus in **albumin** to 1 atom of N there are 4 atoms C; in **gelatin**, $3\frac{1}{2}$ C; in **glycocoll**, 2 C; in **kreatin**, $1\frac{1}{3}$ C; in **uric acid**, $1\frac{1}{4}$ C; in **allantoin**, 1 C; in **urea**, only $\frac{1}{2}$ atom of C. (p. 419).

Circulation of H and O and Salts.—The **H** leaves the body chiefly in the form of **water**—a part, however, is in combination in other excreta; the **O** is chiefly excreted as CO_2 and water; a little is given off in combination in other excreta; **water** is given off by evaporation from the lungs and skin, and also in the urine and fæces. As H is oxidised to H_2O , more water is excreted than is taken in. Most of the readily soluble **salts** are given off by the urine; the less soluble salts, especially those of potash, and the insoluble salts, in the fæces; while others are given off in the sweat. Of the **sulphur** of albumin, about one-half is excreted in the sulphur compounds in the urine, and the other half in the fæces (**taurin**) and in the epidermal tissues.

Every organism has a **minimum** and a **maximum limit** of **metabolism**, according to the amount of work done by the body and its weight. If less food be given than is necessary to maintain the former, the body loses weight; while, if more be given after the maximum limit is reached, the food so given is not absorbed, but remains as a floating balance, and is given off with the fæces. When food is liberally supplied, and the weight increases, of course the minimum limit rises; hence, during the process of “feeding” or “fattening” the amount of food necessary is very much greater than in poorly fed animals, for the same increase of the body-weight. By continuing the process a condition is at last reached in which the digestive organs are just sufficient to maintain the existing condition, but cannot act so as to admit of new additions being made to the body-weight (*v. Bischoff, v. Voit, v. Pettenkofer*).

By the term “**luxus consumption**” is meant the direct combustion or oxidation of the superfluous food-stuffs absorbed by the blood. This, however, does not exist. On the contrary, the material in the juices is always being used for building up the tissues. The albumin found in the fluids, which everywhere permeate the tissues, has been called “**circulating albumin**,” and according to v. Voit it undergoes decomposition sooner than the organised or “**organic albumin**” which forms

an integral part of the tissue. According to v. Voit, in 24 hours 1 per cent. of the organic and 70 per cent. of the circulating albumin is used up.

[Liebig taught that the nitrogenous metabolism of the body depended on a corresponding decomposition of the proteids of the organs, so that the proteids in the food supplied the place of the proteids of the organs thus used up. He called the proteids "**plastic foods**" or "**tissue-formers**," while he regarded the fats and carbohydrates as "**respiratory foods**," as he supposed that they alone were concerned in the evolution of heat. As a matter of fact, experiment proved that the N metabolism is to a large extent independent of the proteids of the food. The *luxus-consumption* theory was invented to explain this. It simply means, that proteids taken with the food not only replace the amount of proteids which have been decomposed during the activity of organs and tissues, but that any excess is immediately consumed without being converted into tissue, and thus this surplus amount giving rise to heat by being oxidised, to a certain extent replaces the fats and carbohydrates. Voit tried to show that nitrogenous metabolism is not influenced by the activity of the organism, and that in ordinary conditions only a small amount of the organic albumin, *i.e.*, that composing tissues and organs, undergoes decomposition, while, owing to the action of the cellular elements of the tissue, a large amount of the circulating albumin is split up, so that, under ordinary conditions, the organic albumin is comparatively stable. This view, he thought, gained support from a comparison of the urea excreted, for the urea may be taken as an index of the N metabolism in well-fed, fasting, and starving animals.]

[It is highly doubtful, however, whether we can draw a sharp distinction between "tissue proteids" and "circulating proteids" as fulfilling two different functions. Formerly the blood was supposed to be the seat of oxidation, but we have seen reason to believe that these processes occur in the tissues. This being so, it seems evident that the food does not undergo decomposition or katabolic changes until it has been assimilated, or become part and parcel of the living tissues, so that the metabolic products are not, as a rule, derived from the food direct, but from the activity of the living tissues. If an increased quantity of food be taken, the excretion of waste products is also increased. On Voit's doctrine of "tissue proteids" and "circulating proteids," part of the proteid was supposed to pass into the blood, and not to be built up into tissues at all, but was oxidised directly in the blood to yield heat only. The theory of "*luxus-consumption*" was invented by Voit to account for this supposed process, because it seemed a wasteful expenditure of proteids. This theory, however, has found but little favour, as so many facts are against it; for the formation of metabolites seems to be essentially a function of living material, *viz.*, the living tissues and organs of the body.]

Quality and Quantity of the Diet for a healthy adult.—As far as his organisation is concerned, man belongs to the **omnivorous** animals, *i.e.*, those that can live upon a mixed diet. For an **adequate diet** man requires for his existence and to maintain health a mixture of the following **four** chief groups of food-stuffs, along with the necessary relishes; none of them must be absent from the food for any length of time. They are:—

1. **Water**—for an adult in his food and drink, 2700 to 2800 grms. (70 to 90 oz. daily (§ 229 and § 247, 1).

[**Thirst.**—The needs of the economy for water are expressed by the sensation of thirst. The sensation of heat and dryness may be confined to the tongue, mouth, and fauces, and indeed may be excited by inhaling dry air. This **local** thirst may be allayed by swallowing water or by eating substances which excite the secretion of saliva. More frequently, however, the sensation is the expression of a **general** condition indicating the diminution of water in the tissues; or it may be due to excess of saline matters in the blood. In some diseases this sensation is very intense, *e.g.*, diabetes. If water be injected into the blood-vessels, or stomach, both the general and local thirst are abolished, even although no water enters the mouth.]

2. **Inorganic substances** or **Salts** are an integral part of all tissues, and without them the tissues cannot be formed. They occur in ordinary food. The addition of too much salt increases the consumption of water, and this in turn increases the transformation of N in the body. If an animal be deprived of salts, nutrition is interfered with; food deprived of its lime affects the formation of the bones; deprivation of common salt causes albuminuria (247, A, III). The alkaline salts serve to neutralise the sulphuric acid formed by the oxidation of the sulphur of the proteids. **Iron**, which is so essential for the formation of blood, exists in animals and plants in combination with complex organic bodies.

Only in times of famine is man driven to eat large quantities of inorganic substances, to

extract the organic matter mixed therewith. A. v. Humboldt states, in regard to the inhabitants of the Orinoco, that they eat a kind of earth which contains innumerable infusoria.

3. At least **one** animal or vegetable albuminous body or **proteid** (§§ 248, 250). The proteids are required to replace the used-up nitrogenous tissues, *e.g.*, for muscles. They contain 15–18 per cent. N.

The **proteids** in blood = 20·56 per cent.; muscles, 19·9 per cent.; liver, 11·74 per cent.; brain, 8·63 per cent.; blood-plasma, 7·5 per cent.; milk, 3·94 per cent.; lymph, 2·46 per cent. According to Pflüger and Bohland, a youth of full stature, and 62 kilos. [136 lbs.] weight, decomposes 89·9 grms. of albumin daily.

Asparagin, in combination with gelatin, can replace albumin in the food (*Weiske*), while asparagin alone limits the decomposition of albumin in herbivora but not in carnivora (*J. Munk*). Ammoniacal salts, glyecoll, sarkosin, and benzamid increase with the amount of albumin in the body.

4. At least **one fat** (§ 251), or a digestible **carbohydrate** (§ 252). These chiefly serve to replace the transformed fats and non-nitrogenous constituents. Owing to the large amount of C which they contain, when they undergo oxidation, they form the chief source of the heat of the body (§ 206). Fats and carbohydrates may replace each other in the food, and in inverse proportion too, corresponding to the amount of C which each contains. As far as the mere evolution of heat is concerned, 100 parts of fat = 256 of grape-sugar = 234 of cane-sugar = 221 of dry starch (*Rubner*). A man consumes 210 grms. fat daily.

[5. Every proper diet ought to have a certain degree of **sapidity** or **flavour**. The substances which give this are not useful in the evolution of energy or building up the tissues, but they stimulate the nervous system and excite secretion. They are called “*Genussmittel*” (means of enjoying food) by the Germans, but we have no exact equivalent for this word in English, though the articles themselves are included under our expression “condiments.” These substances are the aromatic matter in roast meat (osmasome), tea, vinegar, salt, mustard, pepper, &c.]

[**Condition of Diet for Health.**—In an adequate diet, not only (1) should the total quantity of food be sufficient and not more than sufficient, but (2) the constituents should exist in proper proportions, (3) be digestible, and (4) the whole should be in good condition, wholesome, and not adulterated with any substance prejudicial to health.]

With regard to the **relative proportions** of the various kinds of food which ought to be taken, experience has shown that the diet best suited for the body must contain 1 *part of nitrogenous foods to 3½ or, at most, 4½ of the non-nitrogenous*. Looking at ordinary foods from this point of view, we see how far they correspond to this requirement, and how several substances may be combined to produce a satisfactory diet.

Nit. Non-Nit.		Nit. Non.-Nit.		Nit. Non-Nit.	
1. Veal,	10 1	8. Pork,	10 30	14. Barley-meal,	10 57
2. Hare's flesh,	10 2	9. Cow's milk,	10 30	15. White	
3. Beef,	10 17	10. Human milk,	10 37	potatoes,	10 86
4. Lentils,	10 21	11. Wheaten		16. Blue „	10 115
5. Beans,	10 22	flour,	10 46	17. Rice,	10 123
6. Peas,	10 23	12. Oat-meal,	10 50	18. Buck-wheat-	
7. Mutton,	10 27	13. Rye-meal,	10 57	meal,	10 130

An examination of this table shows that, in addition to human milk, wheat-flour has the right proportion of nitrogenous to non-nitrogenous substances. A man who tries to nourish himself on beef alone commits as great a mistake as the one who would feed himself on potatoes alone. Experience has taught people that man may live upon milk and eggs, but that in addition to flesh we must eat bread or potatoes, while pulses require fat or bacon.

The diet varies with the **climate** and with the **season of the year**. As the organism must produce more heat in cold latitudes, the inhabitants of northern climates must eat more non-nitrogenous foods, such as fats and sugars or starches, which, on account of the large amount of C they contain, are admirably adapted for producing heat (§ 214, I., 4).

The graphic representation of the composition of foods (fig. 293) shows the relative proportions of the most important food-stuffs, and how they vary from the standard of 1 nitrogenous to $3\frac{1}{2}$ or $4\frac{1}{2}$ non-nitrogenous.

The **absolute amount of food-stuffs** required by an adult in twenty-four hours

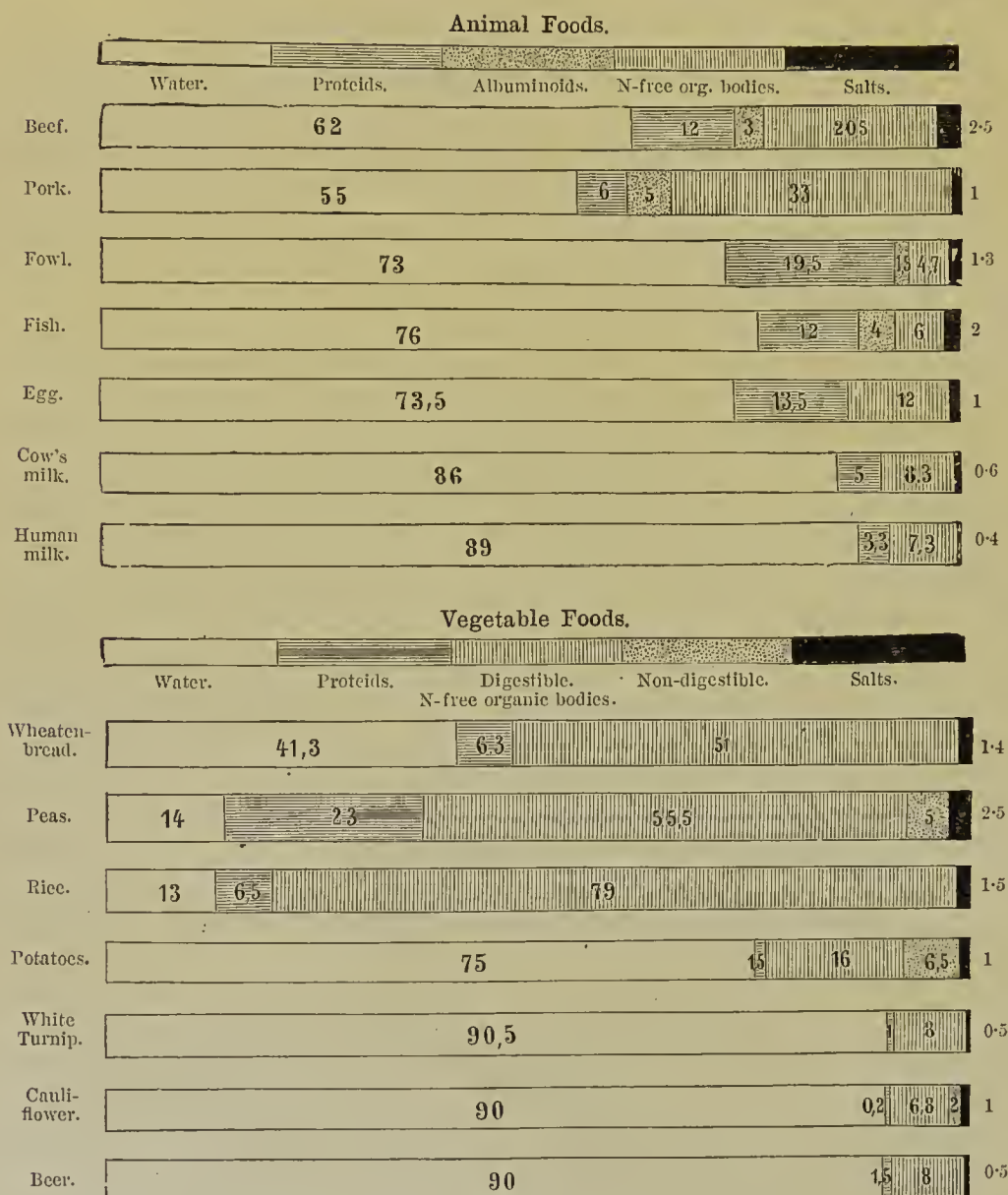


Fig. 293.

depends upon a variety of conditions. As the food represents the chemical reservoir of potential energy, from which the kinetic energy (in its various forms) and the heat of the body are obtained, the absolute amount of food must be increased when the body loses more heat, as in winter, and when more muscular activity (work) is accomplished. As a general rule, *an adult requires daily 130 grams proteids, 84 grams fats, 404 grams carbohydrates, and 30 grams salts.*

A HEALTHY ADULT requires in 24 Hours of water-free solids :—

Food in Grams.	At Rest (<i>Playfair</i>).	Moderate Work (<i>Moleschott</i>).	Laborious Work.	
			(<i>Playfair</i>).	(<i>v. Pettenkofer</i> and <i>v. Voit</i> .)
Proteids, ...	70·87	130	155·92	137
Fats, ...	28·35	84	70·87	117
Carbohydrates (Sugar, Starch, &c.),	310·20	404	597·50	352
Salts, ...	14·00	30	49·00	40

[When we record these numbers in ounces we get the following results as water-free solids required by an average man (*Parkes*) :—

	At Rest.	Ordinary Work.	Laborious Work.
Proteids, ...	2·5	4·6	6 to 7
Fats, ...	1·0	3·0	3·5 to 4·5
Carbohydrates, ...	12·0	14·4	16 to 18
Salts, ...	0·5	1·0	1·2 to 1·5
Total water-free food, ...	16·0	23·0	26·7 to 31·0

During ordinary work the proportion is about :—

Proteids 1 : fats 0·6 : carbohydrates 3·0,
i.e., 1 nitrogenous to 3·6 non-nitrogenous.]

[In a diet for ordinary work (23 oz. of *dry* solids) a man takes about $\frac{1}{100}$ part of his own weight daily ; *ordinary food*, however, as it is consumed, contains between 50 and 60 per cent. of water ; if we add this proportion of water to the actually dry food, we get 48 to 60 oz. of ordinary food (exclusive of liquids). But we consume 50 to 80 oz. of water in some liquid form, making the total amount of water 70 to 90 oz. (*Parkes*).]

The following tables show the elementary composition of the income and expenditure :—

AN ADULT DOING A MODERATE AMOUNT OF WORK takes in :—

	C.	H.	N.	O.
120 grams albumin, containing	64·18	8·60	18·88	28·34
90 „ fats, „	70·20	10·26	...	9·54
330 „ starch, „	146·82	20·33	...	162·85
	281·20	39·19	18·88	200·73

Add 744·11 grm. O from the air by respiration.

„ 2818 „ H₂O.

„ 32 „ Inorganic compounds (salts).

The whole is equal to $3\frac{1}{2}$ kilos. [7 lbs.], i.e., about $\frac{1}{20}$ of the body-weight ; so that about 6 per cent. of the water, about 6 per cent. of the fat, about 1 per cent. albumin, and about 0·4 per cent. of the salts of the body, are daily transformed within the organism.

AN ADULT DOING A MODERATE AMOUNT OF WORK gives off in grams :—

	Water.	C.	H.	N.	O.
By respiration, ...	330	248·8	...	?	651·15
Perspiration, ...	660	2·6	...	...	7·2
Urine, ...	1700	9·8	3·3	15·8	11·1
Fæces, ...	128	20·0	3·0	3·0	12·0
	2818	281·2	6·3	18·8	681·45

Add to this (besides 2818 grams water as drink) 296 grams water formed in the body by the oxidation of H. These 296 grams of water contain 34·89 grms. H, and 263·41 grms. O ; 26 grms. of salts are given off in the urine, and 6 by the fæces. 96·5 grms. of proteid (= 1·46 gm. per kilo.) are used up by a resting adult in twenty-four hours ; but while working 107·6 grms. are used. Nominally 2·3 times as much fat as albumin are used up.

The investigations of the Munich School have shown that the following numbers represent the minimum amount of food necessary for different ages :—

Age.	Nitrogenous.	Fat.	Carbohydrates.
Child until 1½ year, ...	20–36 grms.	30–45 grms.	60–90 grms.
„ from 6 to 15 years, ...	70–80 „	37–50 „	250–400 „
Man (moderate work), ...	118 „	56 „	500 „
Woman „	92 „	44 „	400 „
Old man, ...	100 „	68 „	350 „
Old woman, ...	80 „	50 „	260 „

Small animals have a more lively metabolism than large ones. In small animals the decomposition of albumin per unit weight of body is greater than in large animals (*v. Voit*). Small animals as a rule consume more proteid than larger ones, because they generally have less bodily fat (*Rubner*).

[**Influence of work on the Metabolism.**—When museular work is done in the body, there is a much greater decomposition of **non-nitrogenous** substances in the body, the carbohydrates of musele and the fats of the body are used up, and after they are largely decomposed the museular tissue itself is used up. Pettenkofer and Voit found in an individual weighing 70 kilos (147 lbs.) that his diet (mixed diet) at rest was

Proteids, ...	137 grams	} Containing 19·5 grams N. and 315·5 „ C.
Fats, ...	117 „	
Carbohydrates, ...	352 „	
Water, ...	2262 „	

and he excreted

	Grams N.	Grams C.	Grams Water.
By the urine, ...	17·4	12·6	1194
„ fæces, ...	2·1	14·5	94
„ respiration, ...	...	309·2	1412
Total, ...	19·5	336·3	2700 c.c.

So that his body was in N – equilibrium and he gave off also 438 grams of water and 20·8 grams of C = 28 grams of fat. When, however, he did a large amount of work he took the same amount of proteids and carbohydrates, but nearly double as much fat (§ 294).]

Relation of N to C in Foods and Dietaries.—In most of the ordinary articles of diet, nitrogenous and non-nitrogenous substances are present, but in very varying proportion, in the different foods. Man requires that these shall be in the proportion of 1 : 3½ to 1 : 4½. If food be taken in which this proportion is not observed, in order to obtain the necessary amount of that substance which is contained in too small proportion in his food, he must consume far too much food. In order to obtain the **130 grams of proteids** necessary a person must use

Cheese, ...	388 grms.	Beef, ...	614 grms.	Rice, ...	2562 grms.
Lentils, ...	491 „	Eggs, ...	968 „	Rye-bread, ...	2875 „
Peas, ...	582 „	Wheat-bread, ...	1444 „	Potatoes, ...	10,000 „

provided he were to take only one of these substances as food ; so that if a work-

man were to live on potatoes alone, in order to get the necessary amount of N he would have to consume an altogether excessive amount of this kind of food.

To obtain the **448 grams of carbohydrates**, or the equivalent amount of fat necessary to support him, a man must eat

Rice, ...	572 grms.	Peas, ...	819 grms.	Cheese, ...	2011 grms.
Wheat-bread, ...	625 „	Eggs, ...	902 „	Potatoes, ...	2039 „
Lentils, ...	806 „	Rye-bread, ...	930 „	Beef, ...	2261 „

so that if he were to live upon cheese or flesh alone, he would require to eat an enormous amount of these substances.

In the case of **herbivora**, the proportion of nitrogenous to non-nitrogenous food necessary is 1 of the former to 8 or 9 parts of the latter.

Lastly, all the nutrient material is not necessarily digested and absorbed in the intestinal tract; on the contrary, there always remains an undigested or unused residue which is evacuated with the fæces. The yield of dry substance, with rice as a food, is 4·1 per cent.; white bread, 4·5; flesh, 5·2; egg, 5·2; milk, 9; potatoes, 9·4; peas, 11·8; beans, 18·3; and black bread, 15 (*Prausnitz*) (§ 185, 2).

237. HUNGER AND STARVATION.—If a warm-blooded animal be deprived of all food, it must, in order to maintain the temperature of its body and to produce the necessary amount of mechanical work, transform and utilise the potential energy of the constituents of its own body. The result is that its body-weight diminishes from day to day, until death occurs from starvation.

The following table, from Bidder and Schmidt, shows the amounts in grams of the different excreta in the case of a starved cat:—

Day.	Body-weight.	Water taken.	Urine.	Urea.	Inorganic Substances in Urine.	Dry Fæces.	Expired C.	Water in Urine and Fæces.
1.	2464	...	98	7·9	1·3	1·2	13·9	91·4
2.	2297	11·5	54	5·3	0·8	1·2	12·9	50·5
3.	2210	...	45	4·2	0·7	1·1	13	42·9
4.	2172	68·2	45	3·8	0·7	1·1	12·3	43
5.	2129	...	55	4·7	0·7	1·7	11·9	54·1
6.	2024	...	44	4·3	0·6	0·6	11·6	41·1
7.	1946	...	40	3·8	0·5	0·7	11	37·5
8.	1873	...	42	3·9	0·6	1·1	10·6	40
9.	1782	15·2	42	4	0·5	1·7	10·6	41·4
10.	1717	...	35	3·3	0·4	1·3	10·5	34
11.	1695	4	32	2·9	0·5	1·1	10·2	30·9
12.	1634	22·5	30	2·7	0·4	1·1	10·3	29·6
13.	1570	7·1	40	3·4	0·5	0·4	10·1	36·6
14.	1518	...	41	3·4	0·5	0·3	9·7	38
15.	1434	..	41	2·9	0·4	0·3	9·4	38·4
16.	1389	...	48	3	0·4	0·2	8·8	45·5
17.	1335	...	28	1·6	0·2	0·3	7·8	26·6
18.	1267	...	13	0·7	0·1	0·3	6·1	12·9
	-1197	131·5	773	65·8	9·8	15·7	199·7	734·4

The cat lost 1197 grms. in weight before it died, and this amount is apportioned in the following way:—204·43 grms. (= 17·01 per cent.) loss of albumin; 132·75 grms. (= 11·05 per cent.) loss of fat; 863·82 grms. loss of water (= 71·91 per cent. of the total body-weight lost).

Methods.—In order to investigate the condition of **inanition** it is necessary—(1) to weigh the animal daily; (2) to estimate daily all the C and N given off from the body in the fæces, urine,

and expired air. The N and C, of course, can only be obtained from the decomposition of tissues containing them.

Amongst the general phenomena of inanition, it is found that strong well-nourished dogs die after 4 weeks, man after 21 to 24 days—(6 melancholics who took water died after 41 days); small mammals and birds 9 days, and frogs 9 months. Vigorous adults die when they lose $\frac{1}{10}$ of their body-weight, but young individuals die much sooner than adults. The symptoms are obvious:—The mouth is dry, the walls of the alimentary canal become thin, and the digestive secretions cease to be formed; pulse-beats and respirations are fewer; urine very acid from the presence of an increased amount of sulphuric and phosphoric acids, whilst the chlorine compounds rapidly diminish and almost disappear. The blood contains less water and the plasma less albumin, the gall-bladder is distended, which indicates a continuous decomposition of blood-corpuscles within the liver. The liver is small and very dark coloured, the muscles are very brittle and dry, so that there is a great muscular weakness, and death occurs with the signs of great depression and coma.

Metabolism during inanition.—The relations of the metabolism are given in the foregoing table; the diminution in the excretion of urea is much greater than that of CO_2 , which is due to a larger amount of fats than proteids being decomposed. According to the calculation, there is daily a tolerably constant amount of fat used up, while, as starvation continues, the proteids are decomposed in much smaller amounts from day to day, although the drinking of water accelerates their decomposition.

Excretion of urea during inanition.—The above data shows that the urea excreted falls decidedly during the first few days, then it falls to a minimum, and for several days it remains pretty constant, and then it quickly falls, when the symptoms of approaching death supervene. Sometimes a rise in the quantity excreted takes place when all the fats are used up.]

Loss of Weight of Organs.—It is of importance to determine to what extent the individual organs and tissues lose weight: some undergo simple loss of weight, *e.g.*, the bones; the fat undergoes very considerable and rapid decomposition, while other organs, as the heart, undergo little change, because they seem to be able to nourish themselves from the transformation products of other tissues.

A starving cat, according to v. Voit, lost—

	Per cent. originally present.	Per cent. of the total loss of body-weight.		Per cent. originally present.	Per cent. of the total loss of body-weight.
1. Fat, ...	97	26.2	10. Lungs, . . .	17.7	0.3
2. Spleen, . . .	66.7	0.6	11. Pancreas, . .	17.0	0.1
3. Liver, . . .	53.7	4.8	12. Bones, . . .	13.9	5.4
4. Testicles, . .	40.0	0.1	13. Central Nervous		
5. Muscles, . . .	30.5	42.2	System	3.8	0.1
6. Blood, . . .	37.0	3.7	14. Heart, . . .	2.6	0.02
7. Kidneys, . . .	25.9	0.6	15. Total loss of the		
8. Skin, ...	20.6	8.8	rest of the		
9. Intestine, . .	18.0	2.0	body, ...	36.8	5.0

There is a very important difference according as the animals before inanition have been fed freely on flesh and fat [*i.e.*, if they have a surplus store of food within themselves], or as they have merely had a subsistence diet. Well-fed animals lose weight much more rapidly during the first few days than on the later days. V. Voit thinks that the albumin derived from the excess of food occurs in a state of loose combination in a body as “**circulating**” or “**storage-albumin**,” so that during hunger it must decompose more rapidly and to a greater extent than the “**organic albumin**,” which forms an integral part of the tissues (§ 236). Further, in fat individuals, the decomposition of fat is much greater than in slender persons.

[Comparative.]—Cold-blooded animals live much longer without food than mammals or birds. Snakes may live half a year and frogs nearly a year without food. Dogs may survive for 4 weeks, cats and horses for 3 weeks without food or drink, especially if they are quiet, and not called upon to make any exertion. It is remarkable that small mammals, guinea-pigs and rats survive only for a few days (3–9): rabbits even 19 days. If water be given, however, the animals

survive longer, dogs for 4 weeks, man 4 or 5 weeks, and the dog even 9 weeks. Quite young animals die quicker than adults (*Munk*). As to a human being many factors have to be taken into account,—age (old persons withstand withdrawal of food best), amount of muscular work done, the condition of the atmosphere, whether it is moist and saturated with watery vapour or otherwise; temperature of the surroundings, &c. As a rule, complete abstinence from food and drink cannot be supported for more than 8–10 days, although there are exceptional cases on record where life has been sustained for forty days without food, water, however, being taken. Total deprivation of food in man usually causes death in the third week.]

Zuntz and Lehmann, experimenting on the fasting man Cetti, found that the consumption of O and the production of CO₂ with reference to the unit of body-weight very rapidly reached a minimum, under which it did not fall, although the person continued to starve. As a mean the O consumed on the 3rd to 6th day of starvation = 4.65 e.e. per minute per kilo. The respiratory metabolism diminished very slowly, but not in proportion to the loss of body-weight. At the beginning of starvation the CO₂ fell more rapidly than the O consumed. The respiratory quotient was 0.67. The urea diminished from 1–10 hunger days from 29 to 20 grams.

238. METABOLISM ON A PURELY FLESH DIET.—A man is not able to maintain his metabolism in equilibrium on a purely flesh diet; if he were compelled to live on such a diet, he would succumb. The reason is obvious. In beef the proportion of nitrogenous to non-nitrogenous elementary constituents of food is 1 : 1.7 (p. 441). A healthy person excretes 380 grams [8 to 9 oz.] of carbon in the form of CO₂ in the expired air, and in the urine and faeces. If a man is to obtain 280 grams C from a flesh diet he must consume—digest and assimilate—more than 2 kilos. [4.4 lbs.] of beef in twenty-four hours. But our digestive organs are unequal to this task for any length of time. The person is soon obliged to take less beef, which would necessitate the using of his own tissues, at first the fatty parts, and afterwards the proteid substances.

A carnivorous animal (dog), whose digestive apparatus, being specially adapted for the digestion of flesh—a short intestine and powerfully active digestive fluids—can only maintain its metabolism in a state of equilibrium when fed on a flesh diet free from fat, provided its body is already well supplied with fat, and is muscular. It consumes $\frac{1}{25}$ to $\frac{1}{20}$ part of the weight of its body in flesh, so that the excretion of urea increases enormously. If it eats a larger amount, it may “put on flesh,” when of course it requires more to maintain itself in this condition, until the limit of its digestive activity is reached. If a well-nourished dog is fed on less than $\frac{1}{25}$ to $\frac{1}{20}$ of its body-weight of flesh, it uses part of its own fat and muscle, gradually diminishes in weight, and ultimately succumbs. Poorly fed, non-muscular dogs are unable from the very beginning to maintain their metabolism in equilibrium for any length of time on a purely flesh diet, as they must eat so large a quantity of flesh that their digestive organs cannot digest it. The herbivora cannot live upon flesh food, as their digestive apparatus is adapted solely for the digestion of vegetable food.

[The proteid metabolism depends (1) on the amount of proteids ingested, for the great mass of these becomes changed into circulating albumin; (2) upon the previous condition of nutrition of the organism, for we know that a certain amount of proteid may produce very different results in the same individual when he is in good health, and when he has suffered from some exhausting disease. (3) The use of other foods, *e.g.*, fats and carbohydrates. If a certain amount of fat be added to a diet of flesh, much less flesh is required, so that the N metabolism is reduced by fat. This is spoken of as the “albumin-sparing action of fats.”]

Exactly the same result occurs with other forms of proteids, as with flesh. It has been proved that gelatin may to a certain extent replace proteids in the food, in the proportion of 2 of gelatin to 1 of albumin. The carnivora, which can maintain their metabolism in equilibrium by eating a large amount of flesh, can do so with less flesh when gelatin is added to their food. A diet of gelatin alone, which produces much urea, is not sufficient for this purpose, and animals soon lose their appetite for this kind of food.

[Gelatin.—Voit has shown that gelatin readily undergoes metabolism in the body and forms urea, and if a small quantity be taken, it is completely and rapidly metabolised. When administered it acts just like fats and carbohydrates as an “albumin-sparing” substance. It seems that gelatin is not available directly for the growth and repair of tissues.] Owing to the

great solubility of gelatin, its value as a food used to be greatly discussed. The addition of gelatin in the form of calf's-foot jelly is recommended to invalids. [When a large amount of gelatin is given as food, owing to the large and rapid excretion of urea, the latter excites diuresis.] When chondrin is given along with flesh for a time, grape-sugar is found in the urine.

[The **Metabolism of Peptones**.—Most of the proteids absorbed into the blood are previously converted into peptones by the digestive juices. It has been asserted, more especially by Brücke, that some albumin is absorbed unchanged (§ 192, 4), and that only this is capable of forming organic albumin, while the peptones, after undergoing a reconversion into albumin as they pass through the intestinal wall, undergo decomposition as such.]

239. A DIET OF FAT OR OF CARBOHYDRATES.—If fat alone be given as a food, the animal lives but a short time. The animal so fed excretes even less urea than when it is starving; so that the consumption of fat limits the decomposition of the animal's own proteids. As fat is easily oxidised in the body, it yields heat chiefly, and becomes sooner oxidised than the nitrogenous proteids which are oxidised with more difficulty. If the amount of fat taken be very large, all the C of the fat does not reappear, *e.g.*, in the CO₂ of the expired air; so that the body must acquire fat, whilst at the same time it decomposes proteids. The animal thus becomes poorer in proteids and richer in fats at the same time.

[The **metabolism of fats** is not dependent on the amount of fats taken with the food. 1. It is largely influenced by **work**, *i.e.*, by the activity of the tissues, and in fact with muscular work CO₂ is excreted in greatly increased amount (§ 126, 6). 2. By the **temperature** of the surroundings, as more CO₂ is produced in the cold (§ 214, 2), and far more fatty foods are required in high latitudes. In their action on the organism, proteids and fats so far oppose each other, as the former increase the waste, and therefore oxidation, while the latter diminish it, probably by affecting the metabolic activity of the cells themselves (*Bauer*). As a matter of fact, fat animals or persons bear starvation better than spare individuals. In the latter, the small store of fat is soon used up, and then the albumin is rapidly decomposed. For the same reason corpulent persons are very apt to become still more so, even on a very moderate diet.]

When **carbohydrates alone** are given, they must first be converted by digestion into sugar. The result of such feeding coincides pretty nearly with feeding with fat alone. But the sugar is more easily burned or oxidised within the body than the fat, and 17 parts of carbohydrate are equal to 10 parts of fat. Thus the diet of carbohydrates limits the excretion of urea more readily than a purely fat diet. The animals lose flesh, and appear even to use up part of their own fat.

[The **metabolism of carbohydrates** also serves to diminish the proteid metabolism, as they are rapidly burned up, and thus "spare" or "economise" the circulating albumin. But Pettenkofer and Voit assert that they are rapidly destroyed in the body, even when given in large amount, so that they differ from fats in this respect. They are more easily oxidised than fats, so that they are always consumed first in a diet of carbohydrates and fat. By being consumed they protect the proteids and fats from consumption.]

The direct introduction of grape- and cane-sugar into the blood does not increase the amount of O used, but the amount of CO₂ is increased. [The doctrine of Liebig, that the oxygen taken in is a measure of the metabolic processes, is refuted by these and other experiments. It would seem that fat is not directly oxidised by O, but that it is split up into other simpler compounds which are slowly and gradually oxidised; in fact, fat may lessen the amount of O taken in, as it diminishes waste.]

240. FLESH AND FAT, OR FLESH AND CARBOHYDRATES.—An amount of flesh equal to $\frac{1}{25}$ to $\frac{1}{20}$ of the weight of the body is required to nourish a dog, which is fed on a purely flesh diet; if the necessary amount of fat or carbo-

hydrates be added to the diet, a smaller quantity of flesh is required (*v. Voit*). For 100 parts of fat added to the flesh diet, 245 parts of dry flesh or 227 of syntonin can be dispensed with. If instead of fats carbohydrates are added, then 100 parts of fat = 230 to 250 of the latter (*Rubner*). When the amount of flesh is insufficient, the addition of fat or carbohydrates to the food always limits the decomposition of the animal's own substance. Lastly, when too much flesh is given along with these substances, the weight of the body increases more with them than without them. Under these circumstances, the animal's body puts on more fat than flesh. The **consumption of O** in the body is regulated by the mixture of flesh and non-nitrogenous substances, rising and falling with the amount of flesh consumed. It is remarkable that more O is consumed when a given amount of flesh is taken, than when the same amount of flesh is taken with the addition of fat.

It seems that, instead of fat, the corresponding amount of **fatty acids** has the same effect on the metabolism. [If a dog be fed with fatty acids and a sufficient amount of proteid, no fatty acids are found in the chyle, while fat is formed synthetically, the glycerin for the latter probably being produced in the body (§ 192).] They are absorbed as an emulsion just like the fats. When so absorbed, they seem to be reconverted into fats in their passage from the intestine to the thoracic duct perhaps by the action of the epithelium of the villi. [Glycerin in small doses has no effect on the metabolism of proteid, but in large doses it increases it. It is consumed in the body, as shown by experiments on the respiratory products, and it prevents a certain amount of fat from being used up. About 20 per cent. is excreted in the urine (*Arnschink*). The administration of glycerin to rabbits leads to accumulation of sugar in the liver (p. 318), but, according to Ransom, it inhibits the formation of sugar in the liver, and thus leads to the accumulation of sugar in the liver. The glycosuria that follows injury to the floor of the fourth ventricle is prevented by glycerin, and so is the *post-mortem* change of glycogen into sugar.]

241. STRUCTURE OF ADIPOSE TISSUE AND ORIGIN OF FAT IN THE BODY.—[This tissue is widely distributed in the body; it occurs in subcutaneous tissue as the "panniculus adiposus," around many organs, such as the kidney, and especially in stall-fed animals around the pericardium, in the omentum, under the epicardium, in the yellow marrow of bones, orbital cavities, &c. None is found within the cranium, or in the subcutaneous tissue of the eyelids.

It is a great storehouse of reserve material, and its bulk fluctuates greatly. It is readily formed, and it may be very quickly absorbed again should the needs of the economy require it.

Adipose tissue, when examined microscopically, consists of little bladders or vesicles filled with fat. The vesicles may be spherical or polyhedral from mutual pressure. Each cell is 40–70 μ in diameter and consists of a thin transparent **cell-wall** or envelope, enclosing a large globule of fat, which almost completely fills the cell (fig. 294). At the side, between the cell-wall and the oil-globule, lies the **nucleus**, surrounded by a small quantity of protoplasm. From the nucleus occupying this eccentric position, and when the whole cell is seen from the side, it presents an appearance somewhat like a signet-ring. A thin shell of protoplasm extends round the cell between the envelope and the globule of oil. A fat-cell, therefore, may be regarded as an altered connective-tissue corpuscle, which has become vacuolated, and in the single large vacuole fat is formed. The fat-cells are arranged in **lobules**, and the cells

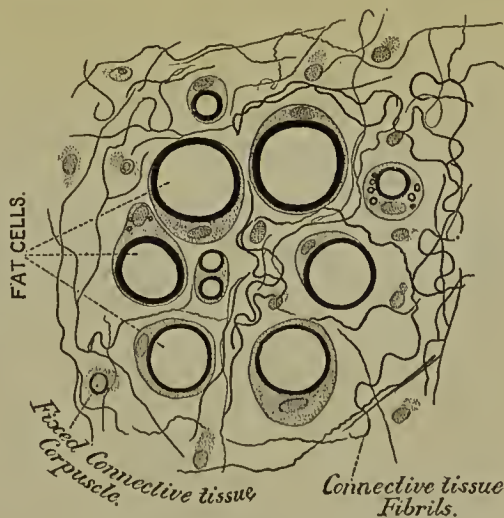
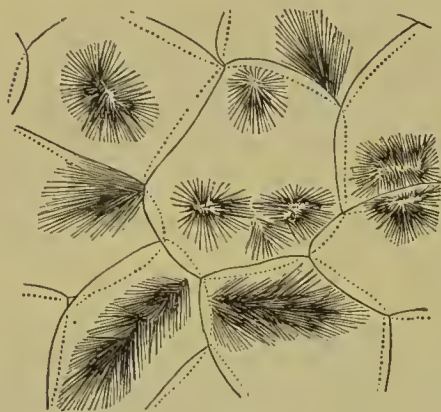


Fig. 294.

Fat-cells from rabbit. $\times 340$.

in each lobule are kept together by a small quantity of connective-tissue. The lobules form larger polygonal lobes. At least one artery and two veins are connected with a lobule, and around the fat-cells is a plexus of capillaries, so that in its general arrangement it assumes a glandular type.]

[**Effect of Reagents on Fat-cells.**—The envelopes are readily brought into evidence by dissolving out the fat by means of hot ether or alcohol. The nucleus



295.

Fat-cells with margarine crystals.

is stained by carmine or logwood, while the fat itself is bleakened by osmic acid. Sometimes after fat-cells are acted on by glycerin, or alcohol, or merely after they are removed from the body, they exhibit a radiate arrangement of crystals of margarine (fig. 295).]

[**Development of Fat-cells.**—Apparently they are derived from modified connective-tissue corpuscles. The corpuscles at first are somewhat spherical, and in their protoplasm small droplets of oil are formed. Gradually these droplets become larger and more numerous, the cell at the same time enlarging, and by and by the droplets run together to form one large globule of oil, so that the remains of the protoplasm and the nucleus are pushed to one side immediately under the cell-wall.]

[**Effect of Starvation.**—Starvation rapidly reduces the amount of fat in the body. The fat-cells gradually and rapidly yield up their fat, and their envelopes remain, diminished, however, in size. The protoplasm may grow somewhat, and in it appear vacuoles filled with a fluid, hence these now altered cells are called “serous fat-cells.”]

I. *Part of the fat of the body is derived directly from the fat of the food, i.e., it is absorbed and deposited in the tissues.* This is shown by the fact that, with a diet containing a small amount of albumin, the addition of more fat causes the deposition of a larger amount of fat in the body (*v. Voit, Hofmann*).

[Hofmann starved a fat dog for 30 days until all its fat was used up. He fed it on lard and a little albumin for 5 days and then killed it. In 5 days it absorbed 1854 grms. of fat and 254 grms. of albumin. It added to its body 1353 grms. of fat; but this amount could not be formed from the proteids of the food, and therefore the fat must have come from the fat of the food. Pettenkofer and Voit arrived at the same result in another way. They fed dogs on flesh and much fat, and by their respiration-apparatus estimated the gaseous income and expenditure (§ 122). *All the N taken in reappeared in the excreta, but not all the C.* The amount of C retained was very large, therefore a non-nitrogenous residue must have been laid up in the body, and it could only be fat, as this was the only substance found in large amount in the body. They estimated the possible amount of fat that could be formed from the proteids, and found that the amount stored up was far greater than this; so that the fat of the food must have been stored up in the tissues.]

Lebedeff found that dogs, which were starved for a month, so as to get rid of all their own fat, on being fed with linseed oil, or mutton suet and flesh, had these fats restored to their tissues. These fats, therefore, must have been absorbed and deposited. J. Munk found the same on feeding animals with rape-seed oil. Fatty acids may also contribute to the formation of fats, as glycerin when formed in the body must be stored up during metabolism (*J. Munk*).

Fatty acids may contribute to the formation of fats by union with the glycerin of the body during the metabolism (p. 369).

II. A second source is the new formation of fats from albuminous bodies. In the case of the formation of fat from proteids, which may yield 11 per cent. of fat (according to Henneberg 100 parts of dry albumin can form 51.5 of fats, together with 33.45 urea, and 27.4 CO₂), these proteids split up into a non-nitrogenous and a nitrogenous atomic compound. The former, provided in a diet containing much albumin, it is not completely oxidised into CO₂ and H₂O, is the substance

from which the fat is formed—the latter leaves the body oxidised chiefly to the stage of urea.

Examples.—That fats are formed from proteids is shown by the following :—1. A cow which produces 1 lb. of butter daily does not take nearly this amount of fatty matter in its food, so that the fat would appear to be formed from vegetable proteids. 2. Carnivora giving suck, when fed on plenty of flesh and *some* fat, yield milk rich in fat. 3. Dogs fed with plenty of flesh and some fat, add more fat to their bodies than the fat contained in the food. 4. Fatty degeneration, *e.g.*, of nerve and muscle, is due to a decomposition of proteids. 5. The transformation of entire bodies, *e.g.*, such as have lain for a long time surrounded with water, into a mass consisting almost entirely of palmitic acid or adipocere is also a proof of the transformation of part of the proteids into fats. 6. Fungi are also able to form fat from albumin during their growth. [7. In starving dogs, Bauer estimated the N and CO₂ given off, and O taken in, and then slowly poisoned them with phosphorus, and he found that the excretion of N was increased twofold, while the excretion of CO₂ and the absorption of O were diminished one-half. Therefore from a large amount of nitrogenous tissue, a nitrogenous body and a small amount of a carbonaceous compound were excreted, while a large amount of a non-nitrogenous residue was retained unconsumed. There was fatty degeneration of all the organs, the fat being derived from the non-nitrogenous part of the proteid. The same obtains with arsenic and antimony.]

Fats not merely absorbed.—Experiments which go to show that the fat of animals, during the fattening process, is not absorbed as such, from the food, are :—1. Fattening occurs with flesh and soaps ; it is most improbable that the soaps are transformed into neutral fats by taking up glycerin and giving up alkali. 2. If a lean dog be fed with flesh and palmitin- and stearin-soda-soap, the fat of its body contains, in addition to palmitin and stearin, *olein* fat, so that the last must be formed by the organism from the proteids of the flesh. Further, Ssnbotin found that when a lean dog was fed on lean meat and spermaceti-fat, a very small amount of the latter was found in the fat of the animal. Although these experiments show that the fat of the body must be formed from the decomposition of proteids, they do not prove that *all* the fat arises in this way, and that none of it is absorbed and redeposited (§ 241, I.).

III. From experiments upon fattening warm-blooded animals (pig, goose, dog) however, Lawes and Gilbert, Lehmann, Heiden, v. Wolff, and others, think they are entitled to conclude that the **carbohydrates** absorbed are *directly* concerned in the formation of fats, a view which is supported by Henneberg, B. Schulze, and Soxhlet. Pigs were fed by Lawes and Gilbert on a large excess of carbohydrates, with very little fat and albumin. In the formation of fat, the converse process takes place, as compared with the formation of glycogen from proteid (§ 174). The molecular group CH . HO, is by reduction changed into CH₂ (*Pflüger*). Suppose the carbohydrate (like albumin) to be decomposed into fat, CO₂ and H₂O, then 100 grms. starch (= 111.1 grms. sugar) at most will yield 41.4 grms. fat, 47.5 grms. CO₂ and 11.4 grms. H₂O (*Meisel*). According to Pasteur, glycerin (the basis of neutral fats) may be formed from carbohydrates.

[Tscherswinsky fed two similar pigs from the same litter ; No. I. weighed 7300 grms.; No. II. 7290 grms. No I. was killed, and its fat and proteids estimated. No. II. was fed for four months on grain and then killed, the grain and excreta and the undigested fat and proteids were analysed, so that the amount of fat and proteid absorbed in four months was estimated. The pig then weighed 24 kilos., it was killed and its fat and proteids estimated.

No. II. contained	2.50 kilos. albumin	and	9.25 kilos. fat.		
No. I.	0.96	„	„	0.69	„ „
Assimilated,	1.56	„	„	8.56	„ „
Taken in in food,	7.49	„	„	0.66	„ „
Difference,	- 5.93	„	„	+ 7.90	„ „

There were therefore 7.90 kilos. of fat in the body which could not be accounted for in the fat of the food. The 5.93 kilos. of albumin of the food which were not assimilated as albumin could yield only a small part of the 7.90 kilos. of fat, so that at least 5 kilos. of fat must have been formed from carbohydrates. Lawes and Gilbert calculated that 40 per cent. of the fat in pigs was derived from carbohydrates. How the carbohydrates are changed into fat in the body is entirely unknown.]

Formerly it was believed that bees could prepare wax from honey alone ; this is a mistake—an equivalent of albumin is required in addition—the necessary amount is found in the raw honey itself.

242. CORPULENCE.—The addition of too much fat to the body is a pathological phenomenon which is attended with disagreeable consequences. With regard to the causes of obesity, without doubt there is an *inherited tendency* (in 33 to 56 per cent. of the cases) in many families—and in some breeds of cattle,—to lay up fat in the body, while other families may be richly supplied with fat, and yet remain lean. The chief cause, however, is taking too much food, *i.e.*, more than the amount required for the normal metabolism; corpulent people, in order to maintain their bodies, must eat absolutely and relatively more than persons of spare habit, under analogous conditions of nutrition (§ 236).

Conditions favouring Corpulence.—(1) A diet rich in *proteids*, with a corresponding addition of *fat* or *carbohydrates*. As flesh or muscle is formed from proteids, and part of the fat of the body is also formed from albumin, the assumption that fats and carbohydrates fatten, or, when taken alone, act as fattening agents, is completely without foundation. (2) *Diminished disintegration* of materials within the body, *e.g.*, (a) *diminished muscular activity* (much sleep and little exercise); (b) *abrogation of the sexual functions* (as is shown by the rapid fattening of castrated animals, as well as by the fact that some women, after cessation of the menses, readily become corpulent); (c) *diminished mental activity* (the obesity of dementia), phlegmatic temperament. On the contrary, vigorous mental work, excitable temperament, care and sorrow, counteract the deposition of fat; (d) *diminished extent of the respiratory activity*, as occurs when there is a great deposition of fat in the abdomen, limiting the action of the diaphragm (breathlessness of corpulent people), whereby the combustion of the fatty matters which become deposited in the body, is limited; (e) a corpulent person requires to use relatively *less heat-giving substances* in his body, partly because he gives off *relatively less heat* from his compact body than is done by a slender long-bodied individual, and partly because the thick layer of fat retards the conduction of heat (§ 214, 4). Thus, corresponding to the relatively diminished production of heat, more fat may be stored up; (f) a *diminution of the red blood-corpuscles*, which are the great exciters of oxidation in the body, is generally followed by an increase of fat—fat people, as a rule, are fat because they have relatively less blood (§ 41)—women with fewer red blood-corpuscles are usually fatter than men; (g) the *consumption of alcohol* favours the conservation of fat in the body, the alcohol is easily oxidised, and thus prevents the fat from being burned up (§ 235).

Disadvantages of corpulence.—Besides the inconvenience of the great size and weight of the body, corpulent people suffer from breathlessness—they are easily fatigued, are liable to intertrigo between the folds of the skin, the heart becomes loaded with fat, and they not unfrequently are subject to apoplexy.

In order to **counteract corpulence** we ought to—(1) *Reduce uniformly all articles of diet*. The diet and body ought to be weighed from week to week, and as long as there is no diminution in the body-weight the amount of food ought to be gradually and uniformly reduced (notwithstanding the appetite). This must be done very gradually and not suddenly. A moderate reduction of fat and carbohydrates in a normal diet at the same time leads to a diminution of the fat of the body itself. Let a person who is capable of muscular exertion take 156 grms. proteid, 43 grms. fat, and 114 grms. carbohydrates; but those in whom congestions, hydræmia, breathlessness have taken place, should take 170 grms. proteid, 25 grms. fat, and 70 grms. carbohydrates (Oertel). It is not advisable to limit the amount of fat and carbohydrates alone, as is done in the **Banting-cure** or Bantingism. Apart altogether from the fact that fat is formed from proteids, if too little non-nitrogenous food be taken, severe disturbance of the bodily metabolism is apt to occur. (2) It is advisable during the chief meal to limit the consumption of fluids of all sorts (even until three-quarters of an hour thereafter), and thus render the absorption and digestive activity of the intestine less active (Oertel). (3) The *muscular activity* ought to be greatly developed by doing plenty of muscular work, or taking plenty of exercise, both physical and mental. (4) *Favour the evolution of heat* by taking cold baths of considerable duration, and afterwards rubbing the skin strongly so as to cause it to become red; further, dress lightly, and at night use light bed-clothing; tea and coffee are useful, as they excite the circulation. (5) Use gentle laxatives: acid fruits, cider; alkaline carbonates (of Marienbad, Carlsbad, Vichy, Neuenahr, Ems, &c.) act by increasing the intestinal evacuations and diminishing absorption. (6) If from accumulation of fat there is danger of failure of the heart's action, Oertel recommends hill-climbing, whereby the cardiac muscle is exercised and strengthened. At the same time the circulation becomes more lively and the metabolism is increased.

[Oertel's Method goes on the idea of strengthening the cardiac musculature, which is sought to be accomplished by (1) limiting the amount of fluids consumed, and (2) carefully regulated muscular exertion. The amount of food is first reduced one-half, and the water to a still lower amount, while the nitrogenous elements in food are increased, the non-nitrogenous are decreased. The person is then instructed to take exercise under certain medical precautions, first, on level ground, and then on gradually increasing gradients.]

Fatty Degeneration.—The process of fattening consists in the deposition of drops of fat within the fat-cells of the panniculus and around the viscera, as well as in the marrow of bone (but they are never deposited in the subcutaneous tissue of the eyelids, of the penis, of the red part of the lips, in the ears and nose). This is quite different from the fatty atrophy or fatty

degeneration which occurs in the form of fatty globules or granules in albuminous tissues, *e.g.*, in muscular fibres (heart), gland-cells (liver, kidney), cartilage-cells, lymph- and pus-corpuscles, as well as in nerve-fibres separated from their nerve-centres. The fat in these cases is derived from albumin, much in the same way as fat is formed in the gland-cells of the mammary and sebaceous glands. Marked fatty degeneration not unfrequently occurs after severe fevers, and after artificial heating of the tissues; when a too small amount of O is supplied to the tissues, as occurs in cases of phosphorus poisoning (*Bauer*); in drunkards; after poisoning with arsenic and other substances, and after some disturbances of the circulation and innervation. Some organs are especially prone to undergo fatty degeneration during the course of certain diseases.

243. METABOLISM OF THE TISSUES.—The **blood-stream** is the chief medium whereby new material is supplied to the tissues and the effete products removed from them. The **lymph** which passes through the thin capillaries comes into actual contact with the tissue elements. Those tissues which are devoid of blood-vessels in their own substance, such as the cornea and cartilage, receive nutrient fluid or lymph from the adjacent capillaries, by means of their cellular elements, which act as juice-conducting media. Hence, when the normal circulation is interfered with, by atheroma or calcification of the walls of the blood-vessels, these tissues are secondarily affected [this, for example, is the case in arcus senilis of the cornea, due to a fatty degeneration of the corneal tissue, owing to some affection of the blood-vessels on which the cornea depends for its nutrition]. Total compression or ligature of *all* the blood-vessels results in necrosis of the parts supplied by the ligatured blood-vessels.

Atrophies caused by diminution of the normal supply of blood, gradually, in the course of time become less and less (*Samuel*).

Hence there must be a *double current* of the tissue juices; the **afferent** or **supply current**, which supplies the new material, and the **efferent stream** which *removes* the effete products. The former brings to the tissues the proteids, fats, carbohydrates, and salts from which the tissues are formed. It is evident that any interruption of the arterial supply to the tissues will diminish this supply.

That such a current exists is proved by injecting an indifferent, easily recognisable substance into the blood, *e.g.*, potassium ferrocyanide, when its presence may be detected in the tissues, to which it has been carried by the outgoing current.

The **efferent stream** carries away the decomposition products *from* the various tissues, more especially urea, CO_2 , H_2O , and salts, and these are transferred as quickly as possible to the organs through which they are excreted.

That such a current exists is proved by injecting such a substance as potassium ferrocyanide into the tissues, *e.g.*, subcutaneously, when its presence may be detected in the urine within two to five minutes.

If the current from the tissues to the blood is so active that the excretory organs cannot eliminate all the effete products from the blood, then these products are found in the tissues. When certain poisons are injected subcutaneously, they pass rapidly into the blood and are carried in great quantity to other tissues, *e.g.*, to the nervous system, on which they act with fatal effect, before they are eliminated to any great extent from the blood by the action of the excretory organs. The effete materials are carried away from the tissues by *two* channels, viz., by the **veins** and by the **lymphatics**, so that if these be interfered with, the metabolism of the tissues must also suffer. When a limb is ligatured so as to compress the veins and the lymphatics, the efferent stream stagnates to such an extent that considerable swelling of the tissues or œdema may occur (§ 203). The action of the muscles and fasciæ are very important in removing these effete matters.

H. Nasse found that the blood of the jugular vein is 0.225 per 1000 specifically heavier than the blood of the carotid, and contains 0.9 part per 1000 more solids; 1000 cubic centimetres of blood circulating through the head yield about 5 cubic centimetres of transudation into the tissues.

The extent and intensity of the metabolism of the tissues depend upon a variety of factors.

1. Their **activity**.—The increased activity of an organ is indicated by the increased amount of blood going to it, and by the more active circulation through it (§ 100). When an organ is completely inactive, such as a paralysed muscle, or the peripheral end of a divided nerve, the amount of blood and the nutritive exchange of fluids diminish within these parts. The parts thus thrown out of activity become pale, relaxed, and ultimately undergo fatty degeneration. The increased metabolism of an organ during its activity has been proved experimentally in the case of **muscle**, and (§ 294) also in the brain (*Speck*). Langley and Sewell have recently observed directly the metabolic changes within sufficiently thin lobules of **glands** during life. The cells of serous glands (§ 143), and those of mucous and pepsin-forming glands (§ 164), during quiescence, become filled with coarse granules, which are dark in transmitted light and white in reflected light, which granules are consumed or disappear during granular activity. During **sleep**, when most organs are at rest, the metabolism is limited; darkness also diminishes it; while **light** excites it, obviously owing to nervous influences. The variations in the total metabolism of the body are reflected in the excretion of CO_2 (§ 126, 9) and urea (§ 257), which may be expressed graphically in the form of a curve corresponding with the activity of the organism; this curve corresponds very closely with the daily variations in the respirations, pulse, and temperature (§ 213, 4).

2. The **composition of the blood** has a marked effect upon the current on which the metabolism of the tissues depends. Very **concentrated** blood, which contains a small amount of water, as after profuse sweating, severe diarrhoea, cholera, makes the tissues dry, while if much water be absorbed into the blood, the tissues become more succulent and even œdema may occur. When much common salt is present in the blood, and when the red blood-corpuscles contain a diminished amount of O, and especially if the latter condition be accompanied by muscular exertion causing dyspnoea, a large amount of albumin is decomposed, and there is a great formation of urea. Hence, exposure to a rarefied atmosphere is accompanied by increased excretion of urea. Certain abnormal conditions of the blood produce remarkable results; blood charged with *carbonic oxide* cannot absorb O from the air, and does not remove CO_2 from the tissues (§ 16). The presence of *hydrocyanic acid* in the blood (§ 16) is said to interrupt at once the chemical oxidation processes in the blood, so that rapid asphyxia, owing to cessation of the *internal* respiration, occurs. Fermentation is interrupted by the same substance in a similar way. A *diminution of the total amount* of the blood causes more fluid to pass from the tissues into the blood, but the absorption of substances—such as poisons or pathological effusions—from the tissues or intestines is delayed. If the substances which pass from the tissues into the blood be rapidly eliminated from it, absorption takes place more rapidly.

3. The **blood-pressure**, when it is greatly increased, causes the tissues to contain more fluid, while the blood itself becomes more concentrated, to the extent of 3 to 5 per 1000. We may convince ourselves that blood-plasma easily passes through the capillary wall, by pressing upon the efferent vessel coming from the chorium deprived of its epidermis, *e.g.*, by a burn or a blister, when the surface of the wound becomes rapidly suffused with plasma. Diminution of the blood-pressure produces the opposite result. The oxidation processes in the body are diminished after the use of P, Cu, ether, chloroform, and chloral.

4. **Increased temperature of the tissues** (several hours daily) does not increase the breaking up of albumin and fats. (See §§ 220, 221, 225.)

5. The **influence of the nervous system** on the metabolism is twofold. On the one hand, it acts indirectly through its effect upon the blood-vessels, by causing them to contract or dilate through the agency of **vaso-motor nerves**, whereby it

influences the amount of blood supplied, and also affects the blood-pressure. But quite independently of the blood-vessels, it is probable that certain special nerves—the so-called **trophic nerves**—influence the metabolism or nutrition of the tissues (§ 342, *c*). That nerves do influence directly the transformation of matter within the tissues is shown by the secretion of saliva resulting from the stimulation of certain nerves, after cessation of the circulation (§ 145), and by the metabolism during the contraction of bloodless muscles. Increased respiration and apnoea are not followed by increased oxidation (*Pflüger*) (§ 126, 8).

[Gaskell has raised the question as to the existence of **katabolic** and **anabolic nerves** controlling respectively the analytic and synthetic metabolism of the tissues.]

244. REGENERATION OF TISSUES AND ORGANS.—The extent to which lost parts are replaced varies greatly in different organs. Amongst the **lower animals**, the parts of organs are replaced to a far greater extent than amongst warm-blooded animals. When a hydra is divided into two parts, each part forms a new individual—nay, if the body of the animal be divided into several parts in a particular way, then each part gives rise to a new individual (*Spallanzani*). The Planarians also show a great capability of reproducing lost parts (*Duges*). Spiders and crabs can reproduce lost feelers, limbs, and claws; snails, part of the head, feelers, and eyes, provided the central nervous system is not injured. Many fishes reproduce fins, even the tail fin. Salamanders and lizards can produce an entire tail, including bones, muscles, and even the posterior part of the spinal cord; while the triton reproduces an amputated limb, the lower jaw, and the eye. This reproduction necessitates that a small stump be left, while total extirpation of the parts prevents reproduction.

In **amphibians** and **reptiles** the regeneration of organs and tissues, as a whole, takes place after the type of the embryonic development, and the same is true as regards the histological processes which occur in the regenerated tail and other parts of the body of the earth-worm. In amphibians and reptiles the same kind of tissue is formed as the tissue which has been injured. The spinal cord is regenerated from the epithelium of the spinal canal. The leucocytes, in the process of new formation, are merely concerned in the nutrition of the parts, and do not enter into their construction (*Fraisse*). [One of the most remarkable cases is the regeneration of the **retina** in tritons after section of the optic nerve (*Griffini*).]

The extent to which regeneration can take place in **mammals** and in **man** is very slight, and even in these cases it is more marked in young individuals. A true regeneration occurs in—

1. The **blood**, including the plasma, the colourless and coloured corpuscles (§ 7 and § 41).

2. The **epidermal appendages** (§ 283) and the **epithelium** of the mucous membranes are reproduced by a proliferation of the cells of the deeper layers of the epithelium, with simultaneous division of their nuclei. Epithelial cells are reproduced as long as the matrix on which they rest and the lowest layer of cells are intact. When these are destroyed cell-regeneration from below ceases, and the cells at the margins are concerned in filling up the deficiency. Regeneration, therefore, either takes place from below or from the margins of the wound in the epithelial covering; leucocytes also wander into the part, while the deepest layer of cells forms large multi-nucleated cells, which reproduce by division polygonal flat nucleated cells. [In the process of division of the cells, the nucleus plays an important part, and in so doing it shows the usual mitotic figures (§ 431).] The **nails** grow from the root forwards; those of the fingers in four to five months, and that of the great toe in about twelve months, although growth is slower in the case of fracture of the bones. The matrix is co-extensive with the *lunule*, and if it be destroyed the nail is not reproduced (§ 284). The **eyelashes** are changed in 100 to 150 days, the other hairs of the body somewhat more slowly. If the papilla of the hair-follicle be destroyed, the hair is not reproduced. Cutting the hair favours its growth, but hair which has been cut does not grow longer than uncut hair. After hair has grown to a certain length, it falls out. The hair never grows

at its apex. The **epithelial cells** of mucous membranes and secretory glands seem to undergo a regular series of changes and renewal. The presence of secretory cells in the milk (§ 231) and in the sebaceous secretion (§ 285) proves this; the spermatozoa are replaced by the action of spermatoblasts. In **catarrhal conditions** of mucous membranes, there is a great increase in the formation and excretion of new epithelium, while many cells are but indifferently formed and constitute mucous corpuscles. The **crystalline lens**, which is just modified epithelium, is reorganised like epithelium; its matrix is the anterior wall of its capsule, with the single layer of cells covering it. If the lens be removed, and this layer of cells retained, these cells proliferate and elongate to form lens fibres, so that the whole cavity of the empty lens capsule is refilled. If much water be withdrawn from the body, the lens fibres become turbid. [A turbid or opaque condition of the lens may occur in diabetes, or after the transfusion of strong common salt or sugar solution into a frog.]

3. The **blood-vessels** undergo extensive regeneration, and they are regenerated in the same way as they are formed (§ 7, B). Capillaries are always the first stage, and around them the characteristic coats are added to form an artery or a vein. When an artery is injured and permanently occluded, as a general rule the part of the vessel up to the nearest collateral branch becomes obliterated, whereby the derivatives of the endothelial lining, the connective-tissue corpuscles of the wall, and the leucocytes change into spindle-shaped cells, and form a kind of cicatricial tissue. Blind and solid outshoots are always found on the blood-vessels of young and adult animals, and are a sign of the continual degeneration and regeneration of these vessels. **Lymphatics** behave in the same way as blood-vessels; after removal of a lymphatic gland, a new lymphatic formation may be produced (*Bayer*).

4. The **contractile substance of muscle** may undergo regeneration after it has become partially degenerated. This takes place after amyloid or wax-like degeneration, such as occurs not unfrequently after typhus and other severe fevers. This is chiefly accomplished by an increase of the muscle corpuscles. After being compressed, the muscular nuclei disappear, and at the same time the contractile contents degenerate. After several days, the sarcolemma contains numerous nuclei which reproduce new muscular nuclei and the contractile substance. In fibres injured by a subcutaneous wound, Neumann found that, after five to seven days, there was a bud-like elongation of the cut ends of the fibres, at first without transverse striation, but with striation ultimately. If a large extent of a muscle be removed, it is replaced by cicatricial connective-tissue. **Non-striped** muscular fibres are also reproduced; the nuclei of the injured fibres divide after becoming enlarged, and exhibit a well-marked intra-nuclear plexus of fibrils. The nuclei divide into two, and from each of these a new fibre is formed, probably by the differentiation of the peri-nuclear protoplasm.

5. After a **nerve** is divided, the two ends do not join at once so as to permit the function of the nerve to be established. On the contrary, marked changes occur. If a piece be cut out of a nerve-trunk, the peripheral end of the divided nerve degenerates, the axial cylinders and the white substance of Schwann disappear. The interval is filled up at first with juicy cellular tissue. The subsequent changes are fully described in § 325, 4. There seems to be in peripheral nerves a continual disappearance of fibres by fatty degeneration, accompanied by a consecutive formation of new fibres (*Sigm. Mayer*). The regeneration of peripheral **ganglionic cells** is unknown. V. Voit, however, observed that a pigeon, part of whose brain was removed, had within five months reproduced a nervous mass within the skull, consisting of medullated nerve-fibres and nerve-cells. Eichhorst and Naunyn found that in young dogs, whose spinal cords were divided between the dorsal and lumbar regions, there was an anatomical and physiological regeneration, to such an extent

that voluntary movements could be executed (§ 338, 3). Vaulair, in the case of frogs, and Masius in dogs, found that mobility or motion was first restored, and afterwards sensibility. Regeneration of the spinal ganglia did not occur. The **taste-bulbs** undergo regeneration after they have undergone degenerative changes following section of the glosso-pharyngeal nerve (*Griffini*).]

6. In many **glands**, the regeneration of their cells during normal activity is very active—sebaceous, mucous, Lieberkühnian, uterine, mammary glands during pregnancy—in others less. If a large portion of a **secretory gland** be removed, as a general rule, it is not reproduced. A gland, if injured, and if suppuration follows, is not regenerated. But the **bile-ducts** (§ 173) and the **pancreatic duct** may be reproduced (§ 171). According to Phillippeaux and Griffini, if part of the **spleen** be removed it is reproduced (§ 103). Tizzoni and Collueci observed the formation of new liver-cells and bile-ducts after injury to the **liver**, and in fact enormous masses of liver may be reproduced (*Griffini, Ponfick*) (§ 173), and Pisenti makes the same statement as regards the **kidney**. After **mechanical injury** to the secretory cells of glands (liver, kidney, salivary, Meibomian), neighbouring cells undergo proliferation, and aid in the restoration of the cells.

7. Amongst connective-tissues, **cartilage**, provided its perichondrium be not injured, reproduces itself by division of its cartilage cells; but usually when a part of a cartilage is removed, it is replaced by connective-tissue.

8. When a **tendon** is divided, proliferation of the tendon cells occurs, and the cut ends are united by connective-tissue.

9. The reproduction of **bone** takes place to a great extent under certain conditions. If the articular end be removed by excision, it may be reproduced, although there is a considerable degree of shortening. Pieces of bone which have been broken off or sawn off heal again, and become united with the original bone. A **tooth** may be removed, replanted in the alveolus, and become fixed there. If a piece of **periosteum** be transplanted to another region of the body, it eventually gives rise to the formation of new bone in that locality. If part of a bone be removed, provided the periosteum be left, new bone is rapidly reproduced; hence, the surgeon takes great care to preserve the periosteum intact in all operations where he wishes new bone to be reproduced. Even the **marrow** of bone, when it is transplanted, gives rise to the formation of bone. This is due to the osteoblasts adhering to the osseous tissue.

In **fracture of a long bone**, the periosteum deposits on the surface of the ends of the broken bones a ring of substance which forms a temporary support, the **external callus**. At first this callus is jelly-like, soft, and contains many corpuscles, but afterwards it becomes more solid and somewhat like cartilage. A similar condition occurs within the bone, where an **internal callus** is formed. The formation of this **temporary callus** is due to an inflammatory proliferation of the connective-tissue corpuscles, and partly to the osteoblasts of the periosteum and marrow. According to Rigal and Vignal, the internal callus is always osseous, and is derived from the marrow of the bone. The outer and inner callus become calcified and ultimately ossified, whereby the broken ends are reunited. Towards the fortieth day, a thin layer of bone is formed (**intermediary callus**) between the ends of the bone. Where this begins to be definitely ossified, the outer and inner callus begin to be absorbed, and ultimately the intermediary callus has the same structure as the rest of the bone.

There are many interesting observations connected with the **growth and metabolism of bones**. 1. The addition of a very small amount of *phosphorus* or *arsenious acid* to the food causes considerable thickening of the bones. This seems to be due to the non-absorption of those parts of the bones which are usually absorbed, while new growth is continually taking place. 2. When food *devoid of lime-salts* is given to an animal, the growth of the bones is not arrested, but the bones become thinner, whereby all parts, even the organic basis of the bone, undergo a uniform diminution. 3. Feeding with **madder** makes the bones red, as the colouring matter is deposited with the bone-salts in the bone, especially in the growing and last-formed parts. In birds the shell of the egg becomes coloured. 4. The continued use of *lactic acid* dissolves the bones. The ash of bone is thereby diminished. If lime-salts be withheld at the same time, the effect is greatly increased, so that the bones come to resemble rachitic bones. (Development of bone, § 447.)

When a lost tissue is not replaced by the same kind of tissue, its place is always taken by **cicatricial connective-tissue**.

When this is the case, the part becomes inflamed and swollen, owing to an exudation of plasma. The blood-vessels become dilated and congested, and, notwithstanding the slower circulation, the amount of blood is greater. The blood-vessels are increased, owing to the formation of new ones. Colourless blood-corpuscles pass out of the vessels and reproduce themselves, and many of them undergo fatty degeneration, whilst others take up nutriment and become converted into large uninucleated protoplasmic cells, from which giant cells are developed. The newly formed blood-vessels supply all these elements with blood.

245. TRANSPLANTATION OF TISSUES.—The nose, ear, and even a finger, after having been severed from the body by a clean cut, have, under certain circumstances, become united to the part from which each was removed. The **skin** is frequently transplanted by surgeons, as, for example, to form a new nose. The piece of skin is cut from the forehead or arm, to which it is left attached by a bridge of skin, is then stitched to the part which it is desired to cover in, and when it has become attached in its new situation, the bridge of skin is severed. Reverdin cut a piece of skin into pieces about the size of a pea and fixed them on an ulcerated surface, where they, as it were, took root, grew, and sent off from their margins epithelial outgrowths, so that ultimately the whole surface was covered with epithelium. [White skin transplanted to a negro ultimately becomes pigmented, and black skin transplanted to a white person becomes white.] The excised *spur* of a cock was transplanted and fixed in the comb of the same animal, where it grew (*John Hunter*). P. Bert cut off the tail and legs of rats and transplanted them under the skin of the back of other rats, where they united with the adjoining parts. Ollier found that, when **periosteum** was transplanted, it grew and reproduced bone in its new situation. Even blood and lymph may be transfused (Transfusion, § 102). [Small portions (1·5 mm.) of epiphyses, costal cartilage, of a rabbit or kitten, when transplanted quite fresh into the anterior chamber of the eye, testis, submaxillary gland, kidney, and under the skin of a rabbit, attach themselves and grow, and the growth is more rapid the more vascular the site on which the tissue is transplanted. Even rabbit's bone has been transplanted to the human subject and grown in its new site. The cartilage is not essentially different from hyaline cartilage, but the cells are fewer in the centre, while the matrix tends to become fibrous. Small pieces of epiphysial cartilage introduced into the jugular vein were found as cartilaginous foci in the lungs. Tissues transplanted from embryonic structures grow far better than adult tissues. If a portion of the **cornea** of a rabbit be transplanted to a human eye, provided Descemet's membrane be clear, it will grow and remain clear (*v. Hippell*). A rabbit's nerve has been transplanted to the human subject, but without success.]

Many of these results seem only to be possible between individuals of the *same species*, although Helferich has recently found that a piece of a dog's muscle, when substituted for human muscle, united to the adjoining muscle, and became functionally active. [Magnus, however, finds that a piece of rabbit's muscle transplanted to another rabbit's muscle serves merely as a temporary structure, and does not unite to the end of the original muscular fibres, but the latter grow and use the transplanted muscle as a scaffolding, which is ultimately absorbed and disappears.] [J. R. Wolfe has transplanted the conjunctiva of the rabbit to the human eye.] Most tissues, however, do not admit of transplantation, *e.g.*, glands and the sense-organs. They may be removed to other parts of the body, or into the peritoneal cavity, without exciting any inflammatory reaction; they, in fact, behave like inert foreign matter.

246. INCREASE IN SIZE AND WEIGHT.—The length of the body, which at birth is usually $\frac{1}{3\frac{1}{5}}$ of the adult body, undergoes the greatest elongation at an

early period :—in the first year, 20 ; in the second, 10 ; in the third, about 7 centimetres ; whilst from five to sixteen years the annual increase is about 5½ centimetres. In the twentieth year the increase is very slight. From fifty onwards the size of the body diminishes, owing to the intervertebral discs becoming thinner, and the loss may be 6 to 7 centimetres about the eightieth year. The **weight of the body** ($\frac{1}{20}$ of an adult) sinks during the first five to seven days, owing to the evacuation of the meconium and the small amount of food which is taken at first. Only on the tenth day is the weight the same as at birth.

The increase of weight is greater in the same time than the increase in length. Within the first year a child trebles its weight. The greatest weight is usually reached about forty, while towards sixty a decrease begins, which at eighty may amount even to 6 kilos. The results of measurements, chiefly by Quetelet, are given in the following table :—

Age.	Length (Cmtr.).		Weight (Kilo.).		Age.	Length (Cmtr.).		Weight (Kilo.).	
	Man.	Woman.	Man.	Woman.		Man.	Woman.	Man.	Woman.
0	49·6	48·3	3·20	2·91	15	155·9	147·5	46·41	41·30
1	69·6	69·0	10·00	9·30	16	161·0	150·0	53·39	44·44
2	79·6	78·0	12·00	11·40	17	167·0	154·4	57·40	49·08
3	86·0	85·0	13·21	12·45	18	170·0	156·2	61·26	53·10
4	93·2	91·0	15·07	14·18	19	170·6	...	63·32	...
5	99·0	97·0	16·70	15·50	20	171·1	157·0	65·00	54·46
6	104·6	103·2	18·04	16·74	25	172·2	157·7	68·29	55·08
7	111·2	109·6	20·16	18·45	30	172·2	157·9	68·90	55·14
8	117·0	113·9	22·26	19·82	40	171·3	155·5	68·81	56·65
9	122·7	120·0	24·09	22·44	50	167·4	153·6	67·45	58·45
10	128·2	124·8	26·12	24·24	60	163·9	151·6	65·50	56·73
11	132·7	127·5	27·85	26·25	70	162·3	151·4	63·03	53·72
12	135·9	132·7	31·08	30·54	80	161·3	150·6	61·22	51·52
13	140·3	138·6	35·32	34·65	90	...	...	57·83	49·34
14	148·7	144·7	40·50	38·10	(Chiefly from Quetelet.)				

Between the 12th and 15th years the weight and size of the girl are greater than of the boy. Growth is most active in the last months of foetal life, and afterwards from the 6th to the 9th year until the 13th to the 16th. The full stature is reached about 30 but not the greatest weight.

General View of the Chemical Constituents of the Organism.

247. (A) INORGANIC CONSTITUENTS.—I. Water forms over 60 per cent. of the whole body, but it occurs in different quantity in the different tissues. The kidneys, brain, and vitreous humour contain the most water ; bones, 22 per cent. ; teeth, 10 per cent. ; while enamel contains the least, 0·2 per cent. (§ 229). According to some observers, *peroxide of hydrogen* (H₂O₂) is also present in the body.

[Approximately, **water** forms about two-thirds of the weight of the body, so that a body weighing 75 kilos. (165 lbs.) contains 50 kilos. (110 lbs.) of water.

The following table, modified from Beaunis, shows the percentage of water in several tissues and organs :—

Solids.								
Tissue or Organ.	Water.	Solids.	Tissue or Organ.	Water.	Solids.	Tissue or Organ.	Water.	Solids.
Enamel, . . .	2	99·8	Spinal cord, . .	69·7	30·3	Thymus, . . .	77·0	23·0
Dentine, . . .	10·0	90·0	White matter } of brain, . .	70·0	30·0	Connective-tissue, . .	79·6	20·4
Bone, . . .	48·6	51·4	Skin, . . .	72·0	28·0	Kidney, . . .	82·7	17·3
Fat, . . .	29·9	70·1	Brain, . . .	75·0	25·0	Grey matter } of brain, . .	85·8	14·2
Elastic tissue, . .	49·6	50·4	Muscles, . . .	75·7	24·3	Vitreous humour, . .	98·7	1·3
Cartilage, . . .	55·0	45·0	Spleen, . . .	75·8	24·2			
Liver, . . .	69·3	30·7						

Liquids.

Blood, . . .	79·1	20·9	Lymph, . . .	95·8	4·2	Aqueous humour, . .	98·6	1·4
Bile, . . .	86·4	13·6	Serum, . . .	95·9	4·1	Cerebro-spinal } fluid, . .	98·8	1·2
Milk, . . .	89·1	10·9	Gastric juice, . .	97·3	2·7	Saliva, . . .	99·5	0·5
Liquor sanguinis, . .	90·1	9·9	Intestinal juice, . .	97·5	2·5	Sweat, . . .	99·5	0·5
Chyle, . . .	92·8	7·2	Tears, . . .	98·2	1·8			

II. Gases.—O, —ozone (§ 37) —H, —N, —CO₂ (§ 38). Marsh gas CH₄ (§ 124), NH₃ (§ 30, § 124, § 184), H₂S (§ 184).

III. Salts.—Sodium chloride [is one of the most important inorganic substances present in the body. It occurs in all the tissues and fluids of the body, and plays a most prominent part in connection with the diffusion of fluids through membranes, and its presence is necessary for the solution of the globulins (p. 465). Sometimes it exists in a state of combination with proteid bodies, as in the blood-plasma. Common salt is absolutely necessary for one's existence as it facilitates absorption by promoting endosmotic processes, and it also increases tissue metabolism; if it be withdrawn entirely, life soon comes to an end. The body contains about 200 grams. About 15 grams are given off in twenty-four hours, chiefly by the urine. Boussingault showed that the addition of common salt to the food of cattle greatly improved their condition].

[Calcium phosphate (Ca₃P₂O₈) is the most abundant salt in the body, as it forms more than one-half of our bones, but it also occurs in dentine, enamel, and to a much less extent in the other solids and fluids of the body. Amongst secretions, milk contains relatively the largest amount. In milk it is necessary for forming the calcareous matter of the bones of the infant. It gives bones their hardness and rigidity. It is chiefly derived from the food, and, as only a small quantity is given off in the excretions, it seems not to undergo rapid removal from the body.]

[Sodium phosphate (Na₃PO₄), acid sodium phosphate (Na₂HPO₄), acid potassium phosphate (K₂HPO₄). The sodium phosphate and the corresponding potash salt give most of the fluids of the body their alkaline reaction. The alkaline reaction of the blood-plasma is partly due to alkaline phosphates, which are chiefly derived from the food. The acid sodium phosphate is the chief cause of the acid reaction of the urine. A small quantity of phosphoric acid is formed in the body owing to the oxidation of lecithin, which contains phosphorus.]

[Sodium carbonate (Na₂CO₃) and sodium bicarbonate (NaHCO₃) exist in small quantities in the food, and are formed in the body from the decomposition of the salts of the vegetable acids. They occur in the blood-plasma, where they play an important part in carrying the CO₂ from the tissues to the lungs.]

[Sodium and potassium sulphates (Na₂SO₄ and K₂SO₄) exist in very small quantity in the body, and are introduced with the food, but part is formed in the body from the oxidation of organic bodies containing sulphur.]

[Potassium chloride (KCl) is pretty widely distributed, and occurs specially in muscle, coloured blood-corpuscles, and milk. Calcium fluoride (CaF₂) occurs in small quantity in bones and teeth. Calcium carbonate (CaCO₃) is associated with calcium phosphate in bone, teeth, and in some fluids, but it occurs in relatively much smaller amount. It is kept in solution by alkaline chlorides, or by the presence of free carbonic acid. Ammonium chloride (NH₄Cl).—Minute traces occur in the gastric juice and the urine. Magnesium phosphate (Mg₃P₂O₈) occurs along with calcium phosphate, but in very much smaller quantity.]

Table by Beaunis of the relative proportions of Salts. The figures give the percentage quantities of mineral matters in the ash.

	Heintz.	Staffel.	Breed.	Oidtmann.	C. Schmidt.	Oidtmann.
	Bone.	Muscle of calf.	Brain.	Liver.	Lungs.	Spleen.
Sodic chloride, . . .	...	10.59	4.74	...	13.0	...
Potassic chloride, . . .	...	...	...	...	...	...
Soda, ...	...	2.35	10.69	14.51	19.5	44.33
Potash, ...	...	34.40	34.42	25.23	1.3	9.60
Lime, ...	37.58	1.99	0.77	3.61	1.9	7.48
Magnesia, ...	1.22	1.45	1.23	0.20	1.9	0.49
Ferric oxide, ...	...	...	...	2.74	3.2	7.28
Chlorine, ...	...	...	...	2.58	...	0.54
Fluorine, ...	1.66	...	...	...	...	...
Phosphoric acid (free), . . .	...	...	9.15	...	...	...
Phosphoric acid (combined), . .	53.31	48.13	39.02	50.18	48.5	27.10
Sulphuric acid, ...	...	...	0.75	0.92	1.4	2.54
Carbon dioxide, ...	5.47	...	...	...	...	...
Silicic acid, ...	...	0.81	0.12	0.27	...	0.17
Ferric phosphate, ...	...	...	1.23	...	...	...

Table by Beaunis of the Mineral Matter in Animal Fluids, i.e., the percentage in the ash.

	Verdeil.	Weber.	Weber.	Dahn-hardt.	Porter.	Wilderstein.	Rose.	Porter.
	Blood.	Blood-serum.	Blood-clot.	Lymph.	Urine.	Milk.	Bile.	Fæces.
Sodic chloride, ...	58.81	72.88	17.36	74.48	67.28	10.73	27.70	4.33
Potassic chloride, ...	...	...	29.87	...	...	26.33	...	...
Soda, ...	4.15	12.93	3.55	10.35	1.33	...	36.73	5.07
Potash, ...	11.97	2.95	22.36	3.25	13.64	21.44	4.80	6.10
Lime, ...	1.76	2.28	2.58	0.97	1.15	18.78	1.43	26.40
Magnesia, ...	1.12	0.27	0.53	0.26	1.34	0.87	0.53	10.54
Ferric oxide, ...	8.37	0.26	10.48	0.50	...	0.10	0.33	2.50
Phosphoric acid, ...	10.23	1.73	10.64	1.09	11.21	19.00	10.45	36.03
Sulphuric acid, ...	1.67	2.10	0.09	...	...	2.64	6.39	...
Carbon dioxide, ...	1.19	4.40	2.17	8.20	...	...	11.26	...
Silicic acid, ...	...	0.20	0.42	1.27	4.06	...	0.36	3.13

IV. Free Acids.—Hydrochloric acid (HCl) [occurs free in the gastric juice, but in combination with the alkalies it is widely distributed as ehlorides.] Sulphuric acid (H₂SO₄) [is said to occur free in the saliva of certain gasteropods, as Dolium galea. In the body it forms sulphates, chiefly in combination with soda and potash. The caterpillar of the Puss Moth secretes for defensive purposes a highly acid fluid composed of formic acid and water. The proportion may be 40 per cent. of acid and one-twentieth of a gram may be ejected at once from a mature larva (Poulton).]

V. Bases.—Silicon as silicic acid (SiO₂); manganese; iron, the last forms an integral constituent of hemoglobin [the total quantity in the blood being about 3 grams]. [Iron is readily detected in organs in which it occurs on hardening small parts of the organ in aleobol and then in alcohol containing ammonium sulphide, which makes the iron granules a green colour]. copper (?), (§ 174).

248. (B) ORGANIC COMPOUNDS.—The Albuminous or Proteid Substances.—(1) True Proteids and their Allies are composed of C, H, O, N, and S, and are derived from plants (see Introduction). [The formation of albumin from the elements is accomplished only by plants. What the chemical processes are is quite unknown. We only know that the N is in the first instance obtained from the nitric acid or

ammonia of the soil. The former is probably not used directly as such, but serves, perhaps, for the formation of amides or amido-acids, from which, by the action of non-nitrogenous bodies, proteids are formed.]

[The exact formula of the proteids is unknown, as they have never been obtained sufficiently pure and in such quantity as to admit of an elementary analysis being made. From such analyses as have been made Bunge gives the following formulæ:—

Egg-albumin, ...	C ₂₀₁	H ₃₂₂	N ₂₅	O ₆₆	S ₂
Proteid in hæmoglobin from horse, .	C ₆₈₀	H ₁₀₉₈	N ₂₁₀	O ₂₄₁	S ₂
Globulin from pumpkin seeds, . .	C ₂₉₂	H ₄₈₁	N ₉₀	O ₈₃	S ₂

According to Hoppe-Seyler their general percentage composition is—

	O	H	N	C	S
From	20·9	6·9	15·2	51·5	0·3
To	23·5	7·3	17·0	54·5	2·0]

They exist in almost all animal fluids and tissues, partly in the fluid form, although Brücke maintains that the molecule of albumin exists in a condition midway between a state of imbibition and a true solution—and partly in a more concentrated condition. Besides forming the chief part of muscle, nerve, and gland, they occur in nearly all the fluids of the body, including the blood, lymph, and serous fluids, but in *health* mere traces occur in the sweat, while they are absent from the bile and the urine. Unboiled **white of egg** is the type. In the alimentary canal they are changed into peptones. The chief products derived from their oxidation within the body are CO₂, H₂O, and especially urea, which contains nearly all the N of the proteids.

[The term proteid (*πρωτεῖον*, pre-eminence) was given by Mulder, and is now used as synonymous with the term “albuminous body.”]

Constitution of Proteids.—Their chemical constitution is quite unknown. The N seems to exist in two distinct conditions, partly loosely combined, so as to yield ammonia readily when they are decomposed, and partly in a more fixed condition. According to Pflüger, part of the N in *living* proteid bodies exists in the form of cyanogen. [Loew supports Pflüger's view that the molecule of living (active) albumin differs from that of dead albumin, as he finds that the living protoplasm of certain algæ can reduce silver in very dilute alkaline solutions, which dead protoplasm cannot do.] The proteid molecule is very large, and is a very complex one; a small part of the molecule is composed of substances from the group of *aromatic* bodies (which become conspicuous during putrefaction), the larger part of the molecule belongs to the *fatty* bodies; during the oxidation of albumin fatty acids especially are developed. *Carbohydrates* may also appear as decomposition-products. For the decompositions during digestion, see § 170, and during putrefaction, § 184. The proteids form a large group of closely related substances, all of which are perhaps modifications of the same body. When we remember that the infant manufactures most of the proteids of its ever-growing body from the casein in milk, this last view seems not improbable.

Characters of Proteids.—Proteids, the anhydrides of peptones (§ 166), are **colloids** (§ 191), and therefore do not diffuse easily through animal membranes; they are amorphous and [for the most part] do **not crystallise**, and hence are isolated with difficulty; some are soluble, others are insoluble in water; insoluble in alcohol and in ether; rotate the ray of polarised light to the *left*; when burned they give the odour of burned horn. Various metallic salts and alcohol precipitate them from their solutions; they are **coagulated** by heat, mineral acids, and the prolonged action of alcohol. Caustic alkalies dissolve them (yellow), and from this solution they are precipitated by acids. By powerful oxidising agents they yield earbamic acid, guanidin, and volatile fatty acids.

Decomposition of proteids.—[The number and varieties of these products are exceedingly great, so that it is not easy to separate the several products. In the first place, there is great difficulty in getting in sufficient quantity a perfectly pure proteid, wherewith to institute the necessary experiments. The decomposition-products of albumin when acted on by barium hydrate have been most fully investigated. The action of concentrated HCl, potassic permanganate, and bromine have also been studied. The action of the animal or vegetable digestive ferments is very important (§ 170), and specially that of bacteria causing putrefaction (§ 184).] When acted upon in a suitable manner by acids and alkalies, they give rise to the decomposition-products—leucin (10 to 18 per cent.), tyrosin (0·25 to 2 per cent.), aspartic acid, glutamic acid, and also volatile fatty acids, benzoic and hydrocyanic acids, and aldehydes of benzoic and fatty

acids; also indol (*Hlasiwetz, Hebermann*). Similar products are formed during pancreatic digestion (§ 170) and during putrefaction (§ 184). [Although it is assumed that the proteids have the closest relation to urea, no one, so far, has succeeded in preparing urea by the direct decomposition of albumin. Both by the action of acids and barium hydrate, the splitting up into simpler compounds does not take place at once, but by successive stages, one to the formation of different bodies. Proteids, when fully decomposed, either by acids or alkalies, yield as the final products ammonia and amido-acids; by alkalies also carbonic, acetic, and oxalic acids. The amido-acids contain several series, including leucin, tyrosin, and glutamic acid. But all proteids do not yield these three bodies, for tyrosin may be absent, while leucin, so far, has been always found. It has therefore been attempted to classify proteids into those that yield tyrosin (*i.e.*, aromatic compounds) and those that do not. Classes I.–VIII., p. 464, yield when decomposed aromatic bodies (tyrosin, indol, phenol), while gelatin-yielding bodies and spongin yield no aromatic bodies.]

[**Electrolysis of Animal Tissues including Proteids.**—A current in passing through a tissue or a proteid solution is conducted almost entirely by the inorganic constituents. The chemical effects produced on the proteid constituents are due to secondary actions of the products of electrolysis of the salts. At the positive pole coagulable proteids are partly coagulated and partly changed into acid-albumin; at the negative pole alkali-albumin is formed. When blood or a pure hæmoglobin solution is electrolysed, methæmoglobin and then acid-hæmatin are formed at the anode, but not if a reducing agent be present; alkali-hæmatin is formed at the cathode (*G. N. Stewart*).]

General Reactions of Proteids.—(1) **Xanthoproteic Reaction.**—Heated with strong nitric acid they give a *yellow*, the addition of excess of ammonia gives a deep *orange* colour. [The deepening of the colour from yellow to orange is the most important part of the reaction and is one of the best tests for the presence of proteids.]

(2) With **Millon's reagent** they give a white precipitate, and when heated with this reagent above 60° C. they give a brick-red colour, probably owing to the formation of tyrosin. [This does not occur in the presence of sodic chloride. If the proteids are present in large amount, a red precipitate occurs, but if mere traces are present only the fluid becomes red.]

(3) **Biuret-reaction.**—The addition of a few drops of a dilute solution of cupric sulphate, and the subsequent addition of excess of caustic potash or soda, give a *violet* colour, which deepens on boiling. The biuret-reaction is so called because the reddish-violet colour is like that given by the substance biuret, a derivative of urea. This is sometimes called **Piotrowski's reaction**. [The same colour is obtained by adding a few drops of Fehling's solution].

(4) They are **precipitated** after strong acidulation by acetic acid and potassium ferrocyanide.

(5) **Liebermann's reaction.**—When proteids are washed with alcohol and ether and then boiled with concentrated hydrochloric acid, they give a violet-red colour.

(6) Sulphuric acid containing molybdic acid gives a blue colour (*Fröhde*).

(7) **Adamkiewicz' reaction.**—Their solution in glacial acetic acid is coloured violet with concentrated sulphuric acid, and shows the absorption-band of hydrobilirubin.

(8) Iodine is a good microscopic reagent, which strikes a brownish-yellow, while sulphuric acid and cane-sugar give a purplish-violet (*E. Schultz*).

[(9) When rendered strongly acid with acetic acid and boiled with an equal volume of a concentrated solution of sodic sulphate, they are precipitated. This method is used for removing proteids from other liquids, as it does not interfere with the presence of other substances. Saturation with sodio-magnesian sulphate precipitates the proteids, but not peptones, and the same is the case with saturation with neutral ammonia sulphate (§ 249).]

[(10) The preecipitation of albumin by *acids* is more delicate when the acid is dissolved in alcohol containing 10 per cent. of ether; the precipitate is not dissolved by an excess of the reagent.]

[(11) Most of them are **precipitated** by strong mineral acids, and metaphosphoric acid, tannic acid (in an acid solution), phosphotungstic and phospho-

molybdic acids (in acid solution); potassio-mercuric iodide (in acid solutions); many metallic salts, *e.g.*, of Cu, Pb, Ag, Hg; chloral, phenol, trichloroacetic acid, picric acid, alcohol. Taurocholic acid precipitates albumin and syntonin, but not peptone or hemi-albumose (§ 181).]

[(12) On adding 2–3 drops of a weak solution of benzaldehyd with a fair amount of sulphuric acid, (1 : 1 water) and 1 drop of ferric sulphate, albumin, on being heated, or after standing, gives a deep blue colour (*Reiche*).

[**Precipitants of Proteids.**—All the proteids cannot be precipitated with equal ease, the albumoses and peptones being exceptions. As a group they are precipitated by (1) strong mineral acids, *e.g.*, nitric, phosphotungstic and metaphosphoric acids; (2) Salts of the heavy metals, forming an albuminate of the metal; (3) acetic acid and ferro-cyanide of potassium; (4) acetic acid and excess of certain neutral salts (NaCl , Na_2SO_4 , MgSO_4); (5) saturation with ammonium sulphate, &c.; (6) picric acid, or tannic acid, or alcohol.]

Proteids may be removed from a fluid containing them by means of (1) Brücke's method, *i.e.*, precipitation with hydrochloric acid and potassio-mercuric iodide (p. 318). (2) By boiling a faintly acid fluid containing them. (3) Wenz's method, *viz.*, saturating the liquid with ammonium sulphate which precipitates all proteids except peptones.]

[**Coagulation of Proteids by Heat.**—When a soluble proteid passes into an insoluble one by heat, this is called heat-coagulation. The proteids coagulated by heat are egg-albumin, serum-albumin, and globulins, but the temperature at which this remarkable change takes place has been shown to vary with the nature of the proteids present in the solution (Fractional heat-coagulation, p. 44) with the concentration of the solution, and also with the quantity and nature of the salts present. The following table after Halliburton shows the temperatures of coagulation of some of the principle proteids :

Albumins.		Globulins.	
Egg-albumin,	73°C	Fibrinogen,	56°C
Serum-albumin α ,	75°	Serum-globulin,	75°
„ „ β ,	77°	Cell-globulin,	75°
„ „ γ ,	84°	Myosinogen,	56°
Cell-albumin,	73°	Myo-globulin,	63°
Muscle albumin,	73°	Vitellin,	75°
Lact-albumin,	77°	Crystallin,	73°]

249. THE ANIMAL PROTEIDS AND THEIR CHARACTERS.—**Class I.**—**Native Albumins** occur in a natural condition in animal solids and fluids. They are **soluble in water** [in dilute saline solutions and in saturated solutions of sodic chloride and magnesium sulphate], and are not precipitated by alkaline carbonates, NaCl , or by very dilute acids. [They are precipitated by saturating their solutions with ammonium sulphate.] Their solutions are coagulated by heating at 65° to 73° C. Dried at 40° C., they yield a clear, yellow, amber-coloured, friable mass, “**soluble albumin**,” which is soluble in water.

(1) **Serum-albumin** (§ 32 and § 41).—Its specific rotatory power is -56° . Almost all its salts may be removed from it by dialysis, when it is no longer coagulated by heat. It is coagulated by strong alcohol; and not very readily precipitated by hydrochloric acid, while the precipitate so formed is easily dissolved on adding more acid. When precipitated, it is readily soluble in strong nitric acid. It is not precipitated when shaken up with ether. The addition of water to the hydrochloric solution precipitates acid-albumin. For its presence abnormally in urine, § 264.

(2) **Egg-albumin.**—When injected into the blood-vessels or under the skin, or even when introduced in large quantity into the intestine, part of it appears unchanged in the urine (§ 192, 4, and § 264). When shaken with ether it is precipitated. These two reactions serve to distinguish it from (1). The specific rotation is -35.5 , *i.e.*, for yellow light. Amount of S, 1.6 per cent.

(3) **Muscle-albumin**, *i.e.*, the proteid extracted from muscle by water (§ 293).

(4) **Cell-albumin** (§ 24).

(5) **Lact-albumin** (§ 231).

Class II.—Globulins are native proteids, insoluble in distilled water, but soluble in dilute neutral saline solutions, *i.e.*, neutral solutions of the alkalis and alkaline earths, *e.g.*, NaCl, KCl, NH_4Cl , Na_2SO_4 , (but not Na_2CO_3 , Na_2PO_4), sodium chloride of 1 per cent., and in magnesium sulphate. [They are insoluble in concentrated solutions of NaCl, MgSO_4 , $(\text{NH}_4)_2\text{SO}_4$.] These solutions are coagulated by heat, and are precipitated by the addition of a large quantity of water. Most of them are *precipitated* from their sodium chloride solution by the addition of crystals of sodium chloride, and also *by saturating their neutral solution at 30° with crystals of magnesium sulphate or ammonium sulphate*. When acted upon by dilute acids they yield acid-albumin, and by dilute alkalis, alkali-albumin.

(1) **Globulin** (Crystallin) is obtained by passing a stream of CO_2 through a watery extract of the crystalline lens.

(2) **Vitellin** is the chief proteid in the yolk of egg. It is also said to occur in the chyle (?) and in the amniotic fluid (*Weyl*). Both the foregoing are not precipitated from their neutral solutions by saturation with sodium chloride.

(3) **Para-globulin** or **Serum-globulin** in blood-plasma (§ 29), and abnormally in urine (§ 264).

(4) **Fibrinogen** (§ 29).—In the clear jelly-like secretion of the vesiculæ seminales of the guinea-pig, there is a globulin-like body closely resembling fibrinogen. It contains 29 per cent. of albumin, with scarcely any ash. If it be touched with a trace of blood-serum, without mixing them, it gradually and completely forms a solid mass quite like fibrin.

(5) **Myosinogen**, from which is formed **myosin**, is the chief proteid in dead muscle. Its coagulation in muscle *post-mortem* constitutes rigor mortis. If muscle be repeatedly washed, and afterward treated with a 10 per cent. solution of sodium or ammonium chloride, it yields a viscid fluid which, when dropped into a large quantity of distilled water, gives a white flocculent precipitate of myosin. It is also precipitated from its NaCl solution by crystals of NaCl. For Kühne's and other methods, see § 293.

(6) **Globin** (*Preyer*), the proteid constituent of hæmoglobin (§ 18).

Class III.—Derived Albumins (Albuminates).—[They are obtained by the action of acids or alkalis on albumins, globulins or other proteids; are insoluble in pure water, but are soluble in acid or alkaline solutions, or in weak saline solutions. Like globulins, they are precipitated by saturation with neutral salts (NaCl , MgSO_4 , $(\text{NH}_4)_2\text{SO}_4$). Their solutions are not coagulated by heat.]

(1) **Acid-albumin** or **Syntonin**.—When proteids are dissolved in the stronger acids, *e.g.*, hydrochloric, they become changed into acid-albumins. They are precipitated from solution by the addition of many salts, sodic chloride, acetate or phosphate, or by neutralisation with an alkali, *e.g.*, sodic carbonate, but they are not precipitated by heat. The concentrated solution gelatinises in the cold, and is redissolved by heat. **Syntonin**, which is obtained by the prolonged action of dilute hydrochloric acid (2 per 1000) upon minced muscle, is also an acid albumin. It is formed also in the stomach during digestion (§ 166, I.). According to Soyka, the alkali- and acid-albumins differ from each other only in so far as the proteid in the one case is united with the base (metal) and in the other with the acid.

(2) **Alkali-albumin**.—If egg- or serum-albumin be acted upon for some time by dilute alkalis, a solution of alkali-albumin is obtained. Strong caustic potash acts upon white of egg, and yields a thick jelly, **Lieberkühn's jelly**. The solution is not precipitated by heat, but it is precipitated by the addition of an acid. [Although alkali-albumin is precipitated on neutralisation, this is not the case in the presence of alkaline phosphates, *e.g.*, sodic phosphate.]

(3) **Casein** is the chief proteid in milk (§ 231). It is precipitated by acids and by rennet at 40° C. In its characters it is closely related to alkali-albuminate, but it contains more N. It contains a large amount of phosphorus (0.83 per cent.). It may be precipitated from milk by diluting it with several times its volume of water and adding dilute acetic acid, or by adding magnesium sulphate crystals to milk and shaking vigorously. Owing to the large amount of phosphorus which it contains, it is sometimes referred to the nucleo-albumins. When it is digested with dilute HCl (0.1 per cent.) and pepsin at the temperature of the body, it gradually yields nuclein.

[**Caseinogen** and **Casein**.—Halliburton has recently suggested that the term caseinogen should be applied to the chief proteid as it exists in milk, reserving the term casein for the precipitate obtained in milk by the action of rennet in the presence of calcium salts. Caseinogen is precipitated from milk by saturating the milk with neutral salts (MgSO_4 , NaCl) or by

adding a very small amount of acid (acetic). This terminology brings the milk-proteid in line with some other proteids, *e.g.*, myosin from myosinogen; fibrin from fibrinogen, &c. Casein, therefore, would be classed "with fibrin, myosin, gluten, as proteids, more or less insoluble, which are produced by ferment action from other proteids of more soluble nature." It is more difficult to classify caseinogen, for in some respects it resembles alkali albumin and in others the globulins, but it differs from both, and Halliburton suggests that it should be put into a class intermediate between the albuminates and the globulins.]

[**Class IV.—Proteoses.**—This name is given to a number of products formed during the hydration of proteids. They are formed by the action of gastric or pancreatic juice on proteids, the final product being peptone. They may also be formed by heating proteids with water, steam, or dilute mineral acids. They are only slightly diffusible. Suppose we start with albumin, before the stage of peptone is reached, an intermediate body, albumose, is formed; this body is a proteose. The particular proteose formed depends on the nature of the original proteid; thus albumin yields albumoses; globulin globuloses; myosin myosinoses, casein caseoses, &c., (§ 166).

They are not coagulated by heat; they are precipitated, but not coagulated by alcohol; with the biuret test they give a rosy pink colour. They are precipitated by nitric acid, but the precipitate is soluble on heating and reappears on cooling.

There are two varieties; suppose we take albumin as the original proteid then we obtain **hemi-albumose**, which can be changed into **hemi-peptone**; and **anti-albumose**, which is changed during digestion into **anti-peptone**.]

[They are classified according to their solubilities into :—

(a) **Proto-albumose**, which is soluble in cold and hot water and saline solutions, but it is precipitated like globulins by saturation with NaCl or MgSO₄.

(b) **Hetero-albumose** is insoluble in water, soluble in 0.5–15 per cent. NaCl solutions in the cold. It is precipitated by dialysing out the salt from its solutions. It is precipitated by saturation with salts.

(c) **Deutero-albumose** is soluble in cold and hot water, not precipitated by saturation with NaCl or MgSO₄, but by ammonium sulphate.

Proto- and hetero-albumose are sometimes called the primary albumoses, while deutero-albumose is a stage much nearer to peptone.

The following table from Halliburton shows the chief properties of these bodies and also of peptone :—

Variety of Proteid.	Hot and Cold Water.	Hot and Cold Saline Solutions, <i>e.g.</i> , 10 per cent. NaCl	Saturation with NaCl or MgSO ₄ .	Saturation with Am ₂ SO ₄ .	Nitric Acid.	Copper Sulphate.	Biuret Test, <i>i.e.</i> , Copper Sulphate and Caustic Potash.
Proto-Albumose	Soluble.	Soluble.	Precipitated.	Precipitated.	Precipitated in cold: precipitate dissolves with heat and reappears on cooling.	Precipitated.	Rose-red colour.
Hetero-Albumose	Insoluble, <i>i.e.</i> , precipitated by dialysis from saline solutions.	Soluble; partly precipitated but not coagulated on heating to 65° C.	Precipitated.	Precipitated.	Do.	Precipitated.	Do.
Deutero-Albumose	Soluble.	Soluble.	Not precipitated.	Precipitated.	This reaction only occurs in presence of excess of salts.	Not precipitated.	Do.
Peptone	Soluble.	Soluble.	Not precipitated.	Not precipitated.	Not precipitated.	Not precipitated.	Do.]

Class V.—Peptones.—There are two classes, **Hemipeptone** and **Antipeptone**. The former can be split up by pancreatic juice into simple products, *e.g.*, leucin and tyrosin (§ 170, II.); the latter not. Nor does the latter give Millon's reaction. Both diffuse readily.

Class VI.—Fibrin.—(§ 72) and for the precursors of fibrin (§ 29).

Class VII.—Coagulated Proteids.—When any native albumins or globulins are coagulated, *e.g.*, at 70° C., they yield bodies with altered characters, insoluble in water and saline solutions, but soluble in boiling strong acids and alkalies, when they are apt to split up. They are dissolved during gastric and pancreatic digestion to produce peptones.

[Halliburton divides coagulated proteids—(1), those coagulated by heat, and (2), those coagulated by the action of ferments. In the latter class is included fibrin, myosin, casein, and anti-albumin.]

Class VIII.—Lardacein and other Bodies.—There fall to be mentioned the “**yelk-plates**,” which occur in the yelk:—**Ichthin** (cartilaginous fishes, frog); **Ichthidin** (osseous fishes); **Ichthulin** (salmon); **Emydin** (tortoise); also the indigestible **amyloid substance** or **lardacein**, which occurs chiefly as a pathological infiltration into various organs, as the liver, spleen, kidneys and blood-vessels. It gives a blue with iodine and sulphuric acid (like cellulose), and a mahogany-brown with iodine. It is difficult to change it into an albuminate by the action of acids and alkalies.

Appendix: Vegetable Proteid Bodies.—Plants, like animals, contain proteid bodies, although in less amount. They occur either in solution in the juices of living plants or in the solid form. In composition and reaction they resemble animal proteids.

[The characters of vegetable proteids have a great resemblance to animal proteids. They have frequently been obtained in a crystalline form, *e.g.*, from the seeds of the gourd and various oleaginous seeds. They occur in greatest bulk in the seeds of plants, **aleurone grains** being for the most part composed of them. In seeds, globulins and “**vegetable peptone**” form the greater proportion of the proteid constituents.]

[**Albumin.**—The existence of a body corresponding to egg- or serum-albumin in the vegetable kingdom is doubtful (*Ritthausen*). Such a body has been described in papaw juice (*Martin*).]

[**Globulins.**—Three varieties have been described as occurring in the seeds of plants:—**vegetable myosin**, **vitellin**, and **paraglobulin** (*Martin*). They have practically the same properties as those found in the animal kingdom: **vegetable vitellin** has, however, not been sufficiently studied. **Paraglobulin** has been found in papaw juice (*Martin*). **Myosin** occurs in the seeds of leguminosæ, in flour, and in the potato. [Globulins are by far the most abundant proteids in plants.]

[**Vegetable Peptone: Albumoses.**—A true peptone has not yet been recognised in plants; what has been described as such is **hemi-albumose** (*Vines*). Albumoses have been found in the seeds of leguminosæ, in flour, and in papaw juice. In the last, two forms occur, called respectively α - and β -**phytalbumose**. The former, α -**phytalbumose**, agrees with the **hemi-albumose** described by Vines, being soluble in cold and boiling water; giving also a biuret-reaction, and a precipitate by saturation with sodium chloride only in an acid solution. The latter, β -**phytalbumose**, is soluble in cold, but not in boiling, distilled water; hence it is precipitated by heat. It is also readily thrown down by saturation with sodium chloride, and gives a faint biuret-reaction (*Martin*).]

[**Vegetable Casein** is said to occur in the seeds of leguminosæ; and it is slightly soluble in water, but readily so in weak alkalies and in solutions of basic calcic phosphate. A solution of this body is precipitated by acids and rennet. Two varieties have been described,—(α) **legumin**, in peas, beans, lentils; acid in reaction, soluble in weak alkalies and very dilute HCl or acetic acid; (β) **conglutin**, a very similar body occurring in hops and almonds. The existence of vegetable casein is denied. Vines states that both legumin and conglutin are artificial products, being formed from the globulins present by the dilute alkali used in extraction of the proteids. This is denied by Ritthausen.]

[**Gluten.**—Gluten is readily prepared from flour by washing and kneading it in a muslin bag under a stream of water. It is probably formed by the fermentation from the proteids pre-existing in flour. So prepared, it is yellowish-brown in colour, very sticky, and capable of being drawn out into long shreds. It is insoluble in water, soluble (but not completely) by prolonged action in dilute acids and alkalies (2 per cent. KHO and HCl). The prolonged action of alcohol (80 to 85 per cent.) dissolves part of the substance of gluten, leaving a residue, called by Liebig **plant-fibrin** and by Ritthausen **gluten-casein**. The alcohol contains **gliadin** (glutin), **gluten-fibrin**, and **mucedin**. **Gluten-casein** is readily soluble in dilute alkalies, almost insoluble in dilute acetic acid, and quite insoluble in cold and boiling water; the products of its decomposition, by heating with H₂SO₄ are leucin, tyrosin, glutamic, and asparaginic acids. The three bodies dissolved from gluten by alcohol differ chiefly in their solubility in alcohol and water. **Gluten-fibrin**, the least soluble, is coagulated by the action of absolute alcohol; it is readily soluble in dilute acids and alkalies, being precipitated by neutralisation.

Gliadin (glutin, plant-gelatin) may be prepared by boiling gluten with water: it deposits on cooling the solution. Though soluble in water at 100° C. at first, it becomes insoluble by the prolonged action of water at that temperature. It is, like gluten-fibrin, soluble in dilute acids and alkalis. **Mucedin** differs from gliadin in being less soluble in strong alcohol. The water used in washing the flour in the preparation of gluten contains hemi-albumose (*Vines*) and a globulin (*Weyl*). Rye-flour, as well as wheaten, yields gluten under similar treatment with water.]

[**Nitrogenous Crystalline Principles.**—Leucin, tyrosin, asparagin, and glutamic acid have been found in the seeds of plants.]

Poisonous Proteids.—Many of the proteids are poisonous, and some of them are the products of the metabolic activity of micro-organisms, which seem to play an important part in the causation of disease. Amongst poisonous animal-proteids are those of snake-poison, *e.g.*, of the cobra and viper which contain [-tox-albumins, -globulins, and -albumoses; the proteids in the serum of the conger eel and other fishes (p. 45), and the albumoses and peptones produced during digestion. Some of the products obtained by cultivating specific bacilli in a culture fluid containing proteid, when injected into an animal, may render that animal immune against an attack of certain diseases. Hankin has shown that an albumose is capable of protecting animals against splenic fever. These bodies are called “**protective proteids.**”]

250. (2) THE ALBUMINOIDS AND FERMENTS.—These substances closely resemble true proteids in their composition and origin, and are amorphous non-crystalline colloids; some of them do not contain S, but the most of them have not been prepared free from ash. Their reactions and decomposition-products closely resemble those of the proteids; some of them produce, in addition to leucin and tyrosin, **glycin** and **alanin** (amido-propionic acid). They occur as organised constituents of the tissues and also in fluid form. It is unknown whether they are formed by oxidation from proteid bodies or by synthesis.

1. **Mucin** is the characteristic substance present in **mucus**. That obtained from the sub-maxillary gland contains—C 52·31, H 7·22, N 11·84, O 28·63. According to Hammarsten, it contains S 1·79 and N 13·5 per cent. It dissolves in water, making it sticky or slimy, and can be filtered. It is precipitated by acetic acid and alcohol; and the alcohol precipitate is again soluble in water. It is not precipitated by acetic acid and ferrocyanide of potassium, but HNO₃ and other mineral acids precipitate it. It gives the xantho-proteid reaction, and becomes red with Millon's reagent. **Occurrence.**—It occurs in saliva (§ 146), in bile, in mucous glands, secretions of mucous membranes, in mucous tissue, in synovia, and in tendons. [The mucin-like body occurring in synovia, which renders synovia viscous, is said by Hammarsten not to be true mucin, but a nucleo-albumin containing 5 per cent. of phosphorus.] Pathologically it occurs not unfrequently in cysts; in the animal kingdom, especially in snails and in the skin of holothurians. It yields leucin and 7 per cent. of tyrosin when it is decomposed by prolonged boiling with sulphuric acid. Mucin behaves like a glucoside; under the action of dilute mineral acids at a high temperature, it splits up into an albuminous body and a carbohydrate (*Labisch*). [The precipitate called mucin has not always the same characters, and, in fact, it differs according to the animal from which it is obtained (*Landwehr*). The so-called mucin of bile is probably a nucleo-albumin (§ 177).]

2. **Nuclein** (§ 24).—*Miescher* gives the formula C₂₅H₄₉N₉P₃O₂₂—contains phosphoric acid, which cannot be separated from it in the cold by dilute neutral acids. It is slightly soluble in water, easily in ammonia, alkaline carbonates, strong HNO₃. It occurs in the nuclei of pus and blood-corpuscles (§ 22), in spermatozooids, yolk-spheres, liver, brain, and milk, yeast, fungi, and many seeds. It has resemblances to mucin, and is perhaps an intermediate product between albumin and lecithin (*Hoppe-Seyler*). It is prepared by the artificial digestion of pus, when it remains as an indigestible residue; acids precipitate it from an alkaline solution. It gives a feeble xantho-proteid reaction; after the prolonged action of alkalis and acid, substances similar to albumin and syntonin are formed. Hypoxanthin and guanin have been obtained as decomposition-products from it (*Kossel*). [A product intermediate between nuclein and hypoxanthin is adenin.]

3. **Keratin** occurs in all horny and epidermic tissues (epidermic scales, hairs, nails, feathers)—C 50·3–52·5, H 6·4–7, N 16·2–17, O 20·8–25, S 0·7–5 per cent.—is soluble in boiling caustic alkalis, but swells up in cold concentrated acetic acid. When decomposed by H₂SO₄ it yields 10 per cent. leucin and 3·6 per cent. tyrosin. **Neuro-keratin** (§ 321).

4. **Fibroin** is soluble in strong alkalis and mineral acids, in ammonio-sulphate of copper;

when boiled with H_2SO_4 it yields 5 per cent. tyrosin, lencin, and glycine. It is the chief constituent of the cocoons of insects and threads of spiders.

5. **Spongin**, allied to fibroin, occurs in the bath-sponge, and yields, as decomposition-products, lencin and glycine (*Stadeler*).

6. **Elastin**, the fundamental substance in elastic tissue, is soluble only when boiled in concentrated caustic potash—C 55-55.6, H 7.1-7.7, N 16.1-17.7, O 19.2-21.1 per cent. It yields 36 to 45 per cent. of lencin and $\frac{1}{2}$ per cent. of tyrosin. [When elastin is digested, elastoses are formed.]

7. **Gelatin (Glutin)**, obtained from connective-tissues by prolonged boiling with water; it gelatinises in the cold—C 52.2-50.7, H 6.6-7.2, N 17.9-18.8, S + O 23.5-25 (S 0.7 per cent.). [Some authors state that it contains no sulphur.] [The ordinary connective-tissues are supposed to contain the hypothetical anhydride **collagen**, while the organic basis of bone is called **ossein**.] It rotates the ray of polarised light strongly to the left = -130° . By prolonged boiling and digestion, it is converted into a peptone-like body (**gelatin-peptone**), which does not gelatinise (§ 161, I.). [It swells up, but does not dissolve in cold water; when dissolved in warm water, and tinged with Berlin blue or carmine, it forms the usual coloured mass which is employed by histologists for making fine transparent injections of blood-vessels.] A body resembling gelatin is found in leucæmic blood and in the juice of the spleen (§ 103, I.). When decomposed with sulphuric acid it yields glycine, ammonia, lencin, *but no tyrosin*. [It is precipitated from its solution by alcohol, mercuric chloride, metaphosphoric acid, phosphotungstic acid, taurocholic acid, tannic acid, but the precipitate with the last does not occur when salts are absent. It is readily soluble in dilute acids, even in acetic acid. When boiled with Millon's reagent, it is not coloured red. With cupric sulphate and caustic soda it gives a violet colour, which, on boiling, becomes light red. It gives no colour with concentrated H_2SO_4 and acetic acid.]

[Gelatin, when treated with superheated steam or digested, yields intermediate bodies, analogous to the proteoses, and finally a **gelatin-peptone** is formed (§ 166, III.), which, however, differs from proteid-peptone as follows (*Salkowski*):—

	Proteid Peptone.	Gelatin.	Gelatin-Peptone.
Adamkiewicz' reaction,	Violet.	Yellowish.	Yellowish.
Addition of an equal volume of concentrated H_2SO_4 ,	Dark brown.	Yellow.	Yellow.
Millon's reaction,	Reddish precipitate.	Colourless.	Colourless.
Xantho-proteid reaction,	Deep yellow.	Lemon-yellow.	Lemon-yellow.

[According to the analysis of Hofmeister, the percentage composition of the gelatinous substances varies within the following limits:—

	Gelatin from bone.	Chondrin.	Albumin.
Carbon,	49.3-50.8	47.7-50.2	50.0-55.0
Hydrogen,	6.5-6.6	6.6-6.8	6.6-7.3
Nitrogen,	17.5-18.4	13.9-14.1	15.0-19.0
Sulphur,	0.56?	0.4-0.6?	0.3-2.4
Oxygen,	24.9-26.0	29.0-51.0	19.0-24.0]

8. **Chondrin** occurs in the matrix of hyaline cartilage and between the fibres in fibro-cartilage. It is obtained from hyaline cartilage and the cornea by boiling. [Its solutions gelatinise on cooling.] It occurs also in the mantle of molluscs—C 49.5-50.6, H 6.6-7.1, N 14.4-14.9, S + O 27.2-29 (S 0.4 per cent.). When boiled with sulphuric acid it yields lencin; with hydrochloric acid, and when digested, chondro-glucose (*Meissner*); it belongs to the glucosides which contain N. When acted upon by oxidising reagents it is converted into gelatin (*Brame*). The substance which yields chondrin is called **chondrigen**, which is perhaps an anhydride of chondrin. The following properties of gelatin and chondrin are to be noted:—**Gelatin** is precipitated by tannic acid, mercuric chloride, chlorine water, platinic chloride, and alcohol, but not by acids, alum, or salts of silver, iron, copper, or lead; its specific rotation is = -130° . [Compare these precipitants with those of albumin.] **Chondrin** is precipitated by acetic acid and dilute sulphuric and hydrochloric acids, by alum, and by salts of silver, iron, and lead; its specific rotation = -213° .

[The following table after Halliburton shows the chief reactions of chondrin compared with those of mucin and of gelatin :—

	Chondrin.	Gelatin.	Mucin.
Solubilities.	Insoluble in cold water, alcohol, or ether. Soluble in hot water; such solutions set into a jelly when cold.	Insoluble in cold water, alcohol, or ether. Soluble in hot water; such solutions set into a jelly when cold.	Insoluble in cold water, alcohol, or ether. Insoluble in hot water.
Acetic acid.	Gives a precipitate insoluble in excess.	Gives no precipitate.	Gives a precipitate insoluble in excess.
Mineral acids.	Give a precipitate soluble in excess.	Give no precipitate.	Give a precipitate soluble in excess.
Tannic acid.	Gives a precipitate.	Gives a precipitate.	Gives no precipitate.
Mercuric chloride.	Gives a precipitate.	Gives a precipitate.	Gives no precipitate.
Lead acetate.	Gives a precipitate.	Gives no precipitate.	Gives a precipitate.
Alum.	Gives a precipitate.	Gives no precipitate.	Gives a precipitate.
When decomposed by boiling with dilute mineral acids.	A reducing sugar is formed.	No reducing sugar is formed.	A reducing sugar is formed.

so that chondrin possesses the reactions of gelatin and also those of mucin.]

[9. **Nucleo-albumins** are compounds of proteids (usually globulins) and nuclein, and occur in cell-protoplasm. The mucin-like substance in bile is a nucleo-albumin (§ 177).]

10. **The hydrolytic ferments** have recently been called **enzymes** by W. Kühne, in order to distinguish them from organised ferments, such as yeast. The enzymes, hydrolytic or organic ferments, act only in the presence of water. They act upon certain bodies, causing them to take up a molecule of water. They all decompose hydric peroxide into water and O. They are most active between 30° to 35° C., and are destroyed by boiling, but when dry they may be subjected to a temperature of 100° without being destroyed. Their solutions, if kept for a long time, gradually lose their properties, and undergo more or less decomposition. [It has been proposed to apply the term **zymolysis** to the action of this group of ferments (*S. Lea*).]

(a) **Sugar-forming, amylolytic, or diastatic-ferment** occurs in saliva (§ 148), pancreatic juice (§ 170), intestinal juice (§ 183), bile (§ 180), blood (§ 22), chyle (§ 198), liver (§ 174), and human milk (§ 231). **Invertin** in intestinal juice (§ 183). Almost all dead tissues, organic fluids, and even proteids, although only to a slight degree, may act diastatically. Diastatic ferments are very generally distributed in the *vegetable kingdom*, the best example being diastase.

(b) **Proteolytic, or ferments which act upon proteids.**—Pepsin in gastric juice and in muscles (§ 166), in vetches, myxomyeetes (*Krukenberg*), trypsin in the pancreatic juice (§ 170), a similar ferment in the intestinal juice (§ 183), and urine (§ 264).

(c) **Fat-decomposing** in pancreatic juice (§ 170), in the stomach (§ 166).

(d) **Milk-coagulating rennet, or rennin**, in the stomach (§ 170), and perhaps also in the intestinal juice (?)—(*W. Roberts*).

(e) There are, however, other ferments, *e.g.*, **coagulative ferments**, *e.g.*, fibrin ferment, myosin ferment, and a ferment from *Withania coagulans*.]

[The importance of **fermentative processes** has already been referred to in detail under “Digestion.” **Ferments** are bodies which excite chemical changes in other matter with which they are brought into contact, without apparently

undergoing any change themselves, or at least they do not enter into the composition of the final product. They are divided into two classes:—

- (1) **Unorganised** ; soluble or non-living.
- (2) **Organised**, or living.]

[(1) **The Unorganised Ferments** are those mentioned in the following table. They seem to be nitrogenous bodies, although their exact composition is unknown, and it is doubtful if they have ever been obtained perfectly pure. They are present in many secretions, and are *produced* within the body by the vital activity of the protoplasm of cells. They are termed *soluble* because they are soluble in water, glycerin, and some other substances (§ 148), while they can be precipitated by alcohol and some other reagents. They do not multiply during their activity, nor is their activity prevented by a certain proportion of salicylic acid. They are not affected by oxygen subjected to the compression of many atmospheres (*P. Bert*). They are *non-living*. Their other properties are referred to above.]

[The **unorganised ferments** present in the body, and their actions (*W. Roberts*):—

Fluid or Tissues.	Ferment.	Actions.
Saliva, . . .	1. Ptyalin (§ 148), . . .	Converts starch chiefly into maltose.
Gastric juice, {	1. Pepsin, ... { 2. Milk-curdling, ... 3. Lactic acid ferment, ... 4. Fat-splitting (?), ...	Converts proteids into peptones in an acid medium, certain bye-products being formed (§ 166). Curdles casein of milk. Splits up milk-sugar into lactic acid. Splits up fats into glycerin and fatty acids.
Pancreatic juice {	1. Diastatic or amylase, ... { 2. Trypsin, ... 3. Emulsive (?), ... 4. Fat-splitting or steapsin, ... 5. Milk-curdling, ...	Converts starch chiefly into maltose. Changes proteids into peptones in an alkaline medium, certain bye-products being formed (§ 170). Emulsifies fats. Splits fats into glycerin and fatty acids. Curdles casein of milk.
Intestinal juice, {	1. Diastatic, ... { 2. Proteolytic, ... 3. Invertin, ... 4. Milk-curdling, ...	Does not form maltose, but maltose is changed into glucose (§ 183). Changes fibrin into peptone (?). Changes cane- into grape-sugar. (? in small intestine).
Blood, . . . Chyle, . . . Liver (?), . . . Milk, . . . Most tissues, . . .	} Diastatic ferments.	
Muscle, . . . Urine, . . .	} Pepsin and other ferments.	
Blood, . . .	Fibrin ferment.	

[(2) **The Organised** or living ferments are represented by yeast (§ 235). Other living ferments belonging to the schizomycetes, occurring in the intestinal canal, are referred to in § 184. Yeast causes fermentation by splitting up sugar into CO₂ and alcohol (§ 150), but this result only occurs so long as the yeast is *living*. Hence, its activity is coupled with the vitality of the cells of the yeast. If yeast be boiled, or if it be mixed with carbolic or salicylic acid, or chloroform, all of

which destroy its activity, it cannot produce the alcoholic fermentation. As yet no one has succeeded in extracting from yeast a substance which will excite the alcoholic fermentation. All the organised ferments grow and **multiply** during their activity at the expense of the substances in which they occur. Thus the alcoholic fermentation depends upon the "life" of the yeast. They are said to be killed by oxygen subjected to the compression of many atmospheres (*P. Bert*). But it is important to note that Hoppe-Seyler has extracted from *dead* yeast (killed by ether) an unorganised ferment—invertin—which can change cane-sugar into grape-sugar.]

11. **Hæmoglobin**, the colouring-matter of blood, which, in addition to C, H, O, N, and S, contains *iron*, may be taken with the albuminoids or with the pigments (§ 11). [**Hæmocyanin** (§ 32).]

(3) Glucosides containing Nitrogen.

In addition to **chondrin**, the following glucosides containing nitrogen, when subjected to hydrolytic processes, may combine with water, and form sugar and other substances:—

Cerebrin (§ 322) = $C_{57}H_{110}N_2O_{25}$ (*Geoghegan*). [Parcus has shown that cerebrin as originally prepared by W. Müller is a mixture of three bodies, viz., cerebrin, homocerebrin, and encephalin.]

Protagon—C 66.29, H 10.69, N 2.39 P 1.068 per cent. [empirical formula, $C_{160}H_{308}N_5PO_{35}$]—occurs in nerves, and contains phosphorus (§ 322).

Chitin, $2(C_{15}H_{25}N_2O_{10})$, is a glucoside containing nitrogen, and occurs in the cutaneous coverings of arthropoda, and also in their intestine and tracheæ; it is soluble in concentrated acids, *e.g.*, hydrochloric or nitric acid, but insoluble in other reagents. According to Sandwick, chitin is an amin-derivative of a carbohydrate with the general formula $n(C_{12}H_{20}O_{10})$. The **hyalin** of worms is closely related to chitin. (Solanin, amygdalin (§ 202), and salicin, &c., are glucosides of the vegetable kingdom.)

(4) Colouring Matters containing Nitrogen.

Their constitution is unknown, and they occur only in animals. They are in all probability derivatives of hæmoglobin. They are—(1) **Hæmoglobin** with its derivatives:—**hæmatin** (§ 18, A), **myohæmatin** (§ 233, § 292), **histo-hæmatin** (§ 103, IV.), and **hæmatoidin** (§ 20). (2) **Bile-pigments** (§ 177, 3). (3) **Urine-pigments** (except Indican). (4) **Melanin**— $C_{44.2}, H_3, N_{9.9}, O_{42.6}$ —or the black pigment which occurs partly in epithelium (choroid, retina, iris, and in the deep layers of epidermis in coloured races) and partly in connective-tissue corpuscles (Lamina fusca of the choroid). [It is probable that there are several melanins.] [**Turacin** occurs in the red feathers of *Corythaix Buffoni*, Cape lory, or Plantain-Eater. Its ash contains nearly 6 per cent. of copper (*Church*). The reddish spots or parts of feathers burn with a green flame.]

(5) Colouring Matters containing no Nitrogen.

[The **lipochromes** are fatty pigments, and are very numerous. They are soluble in ether, and alcohol-like fats, they give certain absorption bands in the spectrum and yield colour-reactions with iodine or sulphuric acid, or with both these reagents together (§ 384). Amongst them are **lutein**, the yellow pigment of the corpus luteum, **tetronerythrin**, the red pigment in the shell of crustaceans (§ 32), the **chromophanes** of the retinal cones (§ 384), and **visual purple** (§ 384).]

II. Organic Acids free from Nitrogen.

(1) The **fatty acids**, with the formula $C_nH_{2n-1}O(OH)$, occur in the body partly free and partly in combination. Free volatile fatty acids occur in decomposing cutaneous secretions (sweat). In combination, acetic acid and caproic acid occur as amido-compounds in glycine (=amido-acetic acid) and leucine (=amido-caproic

acid). More especially do they occur united with glycerin to form neutral fats, from which the fatty acid is again set free by pancreatic digestion (§ 170, III.).

(2) The acids of the **acrylic acid series**, with the formula $C_nH_{2n-3}O(HO)$, are represented in the body by one acid, **oleic acid**— $C_{18}H_{34}O_2$ —which in combination with glycerin yields the neutral fat olein.

251. Fats.—(1) **Neutral fats** occur very abundantly in animals, but they also occur in all plants; in the latter more especially in the seeds (nuts, almonds, cocoa-nut, poppy), more rarely in the pericarp (olive) or in the root. [The chief neutral fats found in the body are **tripalmitin**, $C_3H_5(O.C_{16}H_{31}O)_3$, **tristearin** $C_3H_5(O.C_{18}H_{35}O)_3$ are solid fats and are held in solution at the temperature of the body by **triolein**, $C_3H_5(O.C_{18}H_{33}O)_3$. **Tributylin**, $C_3H_5(O.C_4H_7O)_3$ is found in butter.] They are obtained by pressure, melting, or by extracting them with ether or boiling alcohol. They contain much less O than the carbohydrates, such as sugar and starch; they give a greasy spot on paper, and when shaken with colloid substances, such as albumin, they yield an **emulsion**. When treated with superheated steam or with certain ferments (p. 307, III.), they take up water and yield **glycerin** and **fatty acids**, and if the latter be volatile they have a rancid odour. Treated with caustic alkalis they also take up water, and are decomposed into glycerin and fatty acids; the fatty acid unites with the alkali and forms a **soap**, while glycerin is set free. The soap-solution dissolves fats.

[The following table from Halliburton indicates some of the differences between the neutral fats of the body :—

Stearin.	Palmitin.	Olein.
$C_3H_5(O.C_{18}H_{35}O)_3$. <i>Melting-point.</i> — 53° – 66° C. <i>Solubilities.</i> —Nearly insoluble in cold alcohol and ether. Soluble in both when hot. <i>Remarks.</i> —The chief constituent of the more solid fats (like mutton suet). It crystallises from alcohol in brilliant quadrangular plates.	$C_3H_5(O.C_{16}H_{31}O)_3$. 45° C. More soluble than stearin in both hot and cold alcohol and ether. More abundant in the adipose tissue of man than stearin. It crystallises in fine needles.	$C_3H_5(O.C_{18}H_{33}O)_3$. 0° C. Easily soluble in both hot and cold alcohol and ether. Dissolves all the solid fats, especially at 30° C, or above; it is thus this fat which holds the other two in solution at the temperature of the body.

Glycerin is a tri-atomic alcohol, $C_3H_5(OH)_3$, and unites with (1) the following monobasic *fatty acids* (those occurring in the body are printed in italics):—

Acids.			Acids.			Acids.		
1. <i>Formic</i> , . . .	CH_2O_2		7. <i>Enanthylic</i> , . .	$C_7H_{14}O_2$		[<i>Margaric</i> , . . .	$C_{17}H_{34}O_2$,	
2. <i>Acetic</i> , . . .	$C_2H_4O_2$		8. <i>Caprylic</i> , . .	$C_8H_{16}O_2$		is a mixture		
3. <i>Propionic</i> , . .	$C_3H_6O_2$		9. <i>Pelargonic</i> , . .	$C_9H_{18}O_2$		of 13 and 14.]		
4. <i>Butyric</i> , . . .	$C_4H_8O_2$		10. <i>Capric</i> , . . .	$C_{10}H_{20}O_2$		14. <i>Stearic</i> , . . .	$C_{18}H_{36}O_2$	
[<i>Isobutyric</i> , . .	$C_4H_8O_2$		11. <i>Laurostearic</i> , .	$C_{12}H_{24}O_2$		15. <i>Arachinic</i> , . .	$C_{20}H_{40}O_2$	
5. <i>Valerianic</i> , . .	$C_5H_{10}O_2$		12. <i>Myristic</i> , . .	$C_{14}H_{28}O_2$		16. <i>Hyänic</i> , . . .	$C_{25}H_{50}O_2$	
6. <i>Caproic</i> , . . .	$C_6H_{12}O_2$		13. <i>Palmitic</i> , . .	$C_{16}H_{32}O_2$		17. <i>Cerotic</i> , . . .	$C_{27}H_{54}O_2$	

The acids form a homologous series with the formula $C_nH_{2n-1}O(OH)$. With every CH_2 added their boiling-point rises 19° . Those containing most carbon are solid, and non-volatile; those containing less C (up to and including 10) are fluid like oil, have a burning acid taste, and a rancid odour. The earlier members of the series may be obtained by oxidation from the later, by CH_2 being removed, while CO_2 and H_2O are formed; thus, propionic acid is obtained from butyric acid. Nos. 13 and 14 are found in human and animal fat, less abundant and more inconstant are 12, 11, 6, 8, 10, 4. Some occur in sweat (§ 287) and in milk (§ 231). Many of them are developed during the decomposition of albumin and gelatin. Most of the above (except 15 to 17) occur in the contents of the large intestine (§ 185).

(2) **Glycerin** also unites with the monobasic **oleic acid**, which also forms a series, whose general formula is $C_nH_{2n-3}O(OH)$; and they all contain 2H less than the corresponding

members of the fatty acid series. The corresponding fatty acids can be obtained from the oleic acid series and *vice versa*. **Oleic acid** (olein-elainic acid), $C_{18}H_{34}O_2$, is the only one found in the organism; united with glycerin, it forms the fluid fat, **olein**. The fat of new-born children contains more glycoride of palmitic and stearic acid than that of adults, which contains more glycoride of oleic acid. Oleic acid also occurs united with alkalies (in soaps) and (like some fatty acids) in the lecithins (§ 23). If **lecithin** be acted on with barium hydrate, we obtain insoluble stearic, or oleic, or palmitic acids and barium oleate, together with dissolved neurin (§ 322, *b*) and baric glycono-phosphate. Lecithin is regarded as glycono-phosphate of neurin, in which in the radical of glycono-phosphoric acid 2 atoms H are replaced by 2 of stearic, palmitic, or oleic acids. It appears as if there were several lecithins, of which the most abundant are the one with stearic acid and that with palmitin+oleic acid radical (*Diakonow*). Lecithin occurs in the blood-corpuscles (§ 23), semen, and nerves. Neurin is constantly present in fungi.

The **neutral fats** [palmitin, stearin (both solid), and olein (fluid)], the glycerides of fatty acids, and of oleic acid, are triple ethers of the triatomic alcohol glycerin. With the neutral fats may be associated **glycono-phosphoric acid**, an acid glycerin ether, formed by the union of glycerin and phosphoric acid, with the giving off of a molecule of water ($C_3H_9PO_6$); it is a decomposition-product of lecithin (§ 23).

(3) The **glycolic acids** (acids of the lactic acid series) have the formula $C_nH_{2n-2}O(OH)_2$. They are formed by oxidation from the fatty acid series by substituting OH (hydroxyl) for one atom of H of the fatty acids. Conversely, fatty acids may be obtained from the glycolic acids. The following acids of this series occur in the body:—

(a) **Carbonic Acid** (oxy-formic acid), $CO(OH)_2$; in this form, however, it forms salts only. Free carbonic acid or carbon dioxide is an anhydride of the same $=CO_2$.

(b) **Glycolic Acid** (oxy-acetic acid), $C_2H_2O(OH)_2$ does not occur free in the body. One of its compounds, **glycin** (glycocoll, amido-acetic acid, or gelatin-sugar), occurs as a conjugate acid, viz., as glycocholic acid in the bile (§ 177, 2), and as hippuric acid in the urine (§ 260). Glycin exists in complex combination in gelatin.

(c) **Lactic Acid** (oxy-propionic acid), $C_3H_4O(OH)_2$, occurs in the body in two isomeric forms—1. The **ethylidene lactic acid**, which occurs in two modifications—as the right rotatory **sarcosolactic acid** (paralactic), a metabolic product of muscle; and as the ordinary optically inactive product of “lactic fermentation,” which occurs in gastric juice, in sour milk (sauerkraut, acid cucumber), and can be obtained by fermentation from sugar (§ 184). 2. The isomer, **ethylene-lactic acid**, occurs in the watery extract of muscles (§ 293).

(d) **Leucic Acid** (oxy-caproic acid), $C_6H_{12}O_3$, does not occur as such, but only in the form of one of its derivatives, **leucin** (amido-caproic acid), as a product of the metabolism in many tissues, and is formed during pancreatic digestion (§ 170, II.). Leucic acid may be prepared from leucin, and glycolic acid from glycin, by the action of nitrous acid.

(4) **Acids of the Oxalic Acid or Succinic Acid Series**, having the formula $C_nH_{2n-4}O_2(OH)_2$, are bi-basic acids, which are formed as completely oxidised products by the oxidation of fatty acids and glycolic acid, water being removed. It is important to note their origin from substances rich in carbon, *e.g.*, fats, carbohydrates, and proteids.

(a) **Oxalic Acid**, $C_2O_2(OH)_2$, arises from the oxidation of glycol, glycin, cellulose, sugar, starch, glycerin, and many vegetable acids—it occurs in the urine as calcium oxalate (§ 260).

(b) **Succinic Acid**, $C_4H_2O_4(OH)_2$, has been found in small amount in animal solids and fluids, spleen, liver, thymus, thyroid; in the fluids of echinococcus, hydrocephalus, and hydrocele, and more abundantly in dog's urine after fatty and flesh food; in rabbit's urine after feeding with yellow turnips. It is also formed in small amount during alcoholic fermentation (§ 150).

(5) **Cholalic Acid** in the bile (§ 177) and in the intestine (§ 182).

(6) **Aromatic Acids** contain the radical of benzol. [Benzene or benzol, with the formula C_6H_6 , is the origin of the aromatic group, so called because many of the derivatives of this body have aromatic properties. One or more of the atoms of hydrogen can be replaced by more or less complicated radicals.] **Benzoic Acid** (=phenyl-formic acid) occurs in urine united with glycin, as hippuric acid (§ 260).

III. Alcohols.

Alcohols are bodies which originate from carbohydrates, in which the radical hydroxyl (HO) is substituted for one or more atoms of H. They may be also regarded as water, $\left. \begin{matrix} H \\ H \end{matrix} \right\} O$, in which the half of the H is replaced by a CH com-

pound. Thus, C_2H_6 (ethyl-hydride) passes into $\left. \begin{matrix} C_2H_5 \\ H \end{matrix} \right\} O$ (ethylic alcohol).

(a) **Cholesterin**, $\left. \begin{matrix} C_{26}H_{43} \\ H \end{matrix} \right\} O$, is a true monatomic alcohol, and occurs in blood, yolk, brain,

bile (§ 177, 4), and generally in vegetable cells; it is the only solid monatomic alcohol in the body.

(b) **Glycerin**, C_3H_5 $\begin{cases} OH \\ OH \\ OH \end{cases}$, is a triatomic alcohol. It occurs in neutral fats united with fatty acids and oleic acid; it is formed by the splitting up of neutral fats during pancreatic digestion (§ 170, III.), and during the alcoholic fermentation (§ 150).

(c) **Phenol** (= phenylic acid, carbolic acid, oxy-benzol) (§ 184, III.).

(d) **Pyrokatechin** (= dioxybenzol) (§ 252).

(e) The **Sugars** are closely related to the alcohols, and they may be regarded as polyatomic alcohols. Their constitution is unknown. Together with a series of closely-related bodies they form the great group of the **carbohydrates**, some of which occur in the animal body, while others are widely distributed in the vegetable kingdom.

252. THE CARBOHYDRATES.—Occur in plants and animals, and receive their name, because in addition to C (at least 6 atoms), they contain H and O, in the proportion in which these occur in water. They are all solid, chemically indifferent, and without odour. They have either a sweet taste (sugars), or can be readily changed into sugars by the action of dilute acids; they rotate the ray of polarised light either to the right or left; as far as their constitution is concerned, they may be regarded as fatty bodies, or as hexatomic alcohols, in which 2H are wanting.

Small quantities of carbohydrates occur in nearly all animal tissues. Under certain conditions of nutrition, there is reason to believe that complex organic constituents of our tissues, *e.g.*, proteids, split up into a nitrogenous body from which urea is readily formed, and a non-nitrogenous carbon-containing residue, and from the latter fat or carbohydrates may be formed (§ 241). Carbohydrates are formed from fats in the germination of oleaginous seeds, oxygen being absorbed in the process.

They are divided into the following groups:—

I. Division.—**Glucoses** ($C_6H_{12}O_6$).—(1) **Grape-sugar** (glucose, dextrose, or diabetic sugar) occurs in minute quantities in the blood, chyle, muscle, liver (?), urine, and in large amount in the urine in diabetes mellitus (§ 175). It is formed by the action of diastatic ferments upon other carbohydrates, during digestion. In the **vegetable kingdom** it is extensively distributed in the sweet juices of many fruits and flowers (and thus it gets into honey). It is formed from cane-sugar, maltose, dextrin, glycogen, and starch, by boiling with dilute acids. It crystallises in warty masses with one molecule of water of crystallisation; unites with bases, salts, acids, and alcohols, but is easily decomposed by bases; it **reduces many metallic oxides** (§ 149). Fresh solutions have a rotatory power of $+106^\circ$. By fermentation with yeast it splits up into alcohol and CO_2 (§ 150); with decomposing proteids it splits into 2 molecules of lactic acid (§ 184, I.); the lactic acid splits up under the same conditions in alkaline solutions, into butyric acid, CO_2 , and H. For the qualitative and quantitative estimation of glucose, see § 149 and § 150. In alcoholic solution, it forms very insoluble compounds with chalk, barium, and potassium, and it also forms a crystalline compound with common salt (Estimation, § 150).

(2) **Galactose**, obtained by boiling milk-sugar (lactose) with dilute mineral acids; it crystallises readily, is very fermentable, and gives all the reactions of glucose. When oxidised with nitric acid it becomes transformed into mucic acid. Its specific rotatory power = $+88.08^\circ$.

(3) **Laevulose** (left-fruit-, invert-, or mucin-sugar) occurs as a colourless syrup in the acid juices of some fruits and in honey; is non-crystallisable, and insoluble in alcohol; specific rotatory power = -106° . It is formed normally in the intestine (§ 183), and occurs rarely as a pathological product in urine.

II. Division.—This contains carbohydrates with the formula $C_{12}H_{22}O_{11}$, and its members may be regarded as anhydrides of the first division—1. **Milk-sugar** or **lactose** occurs only in milk, crystallises in cakes (with 1 molecule of water) from the syrupy concentrated whey; it rotates polarised light to the right = $+59.3$, and is much less soluble in water and alcohol than grape-sugar. When boiled with dilute mineral acids it passes into galactose, and can be directly transformed into lactic acid only by fermentation; the galactose, however, is capable of undergoing the alcoholic fermentation with yeast (Koumiss preparation, § 231). For its quantitative estimation (§ 231). Rare in urine (§ 267).

2. **Maltose** ($C_{12}H_{22}O_{11} + H_2O$ (*O'Sullivan*)) has 1 molecule of water less than grape-sugar ($C_{12}H_{24}O_{12}$), is formed during the action of a diastatic ferment, such as saliva upon starch (§ 148); is soluble in alcohol, right-rotatory power = $+150^\circ$; it is crystalline, while its reducing power is only two-thirds that of dextrose. [The ratio of the reducing power of maltose to that of glucose is 100 to 66.]

(3. **Saccharose** (cane-sugar) occurs in sugar-cane and some plants; it does not reduce a

solution of copper, is insoluble in alcohol, is right-rotatory and not capable of fermentation. When boiled with dilute acids, it becomes changed into a mixture of easily fermentable glucose (right-rotatory) and laevulose (invert sugar, § 183, 5, and § 184, I., 7), which ferments with difficulty and is left-rotatory (§ 183). When oxidised with nitric acid, it passes into glucic acid and oxalic acid.)

III. Division.—This contains carbohydrates, with the formula $(C_6H_{10}O_5)_n$, which may be regarded as anhydrides of the second division.

1. **Glycogen**, with a dextro-rotatory power of 211° , does not reduce cupric oxide. It occurs in the liver (§ 174), muscles, many embryonic tissues, the embryonic area of the chick (*Külz*) in normal and pathological epithelium; in diabetic persons it is widely distributed; brain, pancreas, and cartilage; and in the spleen, pancreas, kidney, ovum, brain, and blood, together with a small amount of glucose (*Pavy*). It also occurs in the oyster and some of the molluscs (*Bizio*), and indeed in all tissues and classes of the animal kingdom.

2. **Dextrin** was discovered by Limpricht in the muscles of the horse. It is right-rotatory = $+138^\circ$, soluble in water, and forms a very sticky solution, from which it is precipitated by alcohol or acetic acid; it is tinged red brown with iodine. It is formed in roasted starch, (hence it occurs in large quantity in the crust of bread—see *Bread*, § 234), from starch by dilute acids, and in the body by the action of ferments (§ 148). It is formed from cellulose by the action of dilute sulphuric acid. It occurs in beer, and is found in the juices of most plants.

(3. **Amylum** or **Starch** occurs in the “meally” parts of many plants, is formed within vegetable cells, and consists of concentric layers with an eccentric nucleus (fig. 186). The diameter and characters of starch-grains vary greatly with the plant from which they are derived. At 72° C. it swells up in water and forms a mucilage; in the cold, iodine colours it blue. Starch-grains always contain more or less cellulose and a substance, **erythrogranulose**, which is coloured red with iodine (§ 148). It and *glycogen* are transformed into dextrose by certain digestive ferments in the saliva, pancreatic, and intestinal juices, and artificially by boiling with dilute sulphuric acid.)

(4. **Gum**, $C_{10}H_{20}O_{10}$ occurs in vegetable juices (especially in acacia and mimosæ), also in the salivary glands, mucous tissue, lungs, and urine; is partly soluble in water (arabin), partly swells up like mucin (bassorin). Alcohol precipitates it. It is fermentable, and when boiled with dilute acid yields a reducing sugar.)

(5. **Inulin**, a crystalline powder occurring in the root of chicory, dandelion, and specially in the bulbs of the dahlia; it is not coloured blue by iodine.)

(6. **Lichenin** occurs in the intercellular substance of Iceland moss (*Cetraria islandica*) and algae; is transformed into glucose by dilute sulphuric acid.)

(7. **Paramylum** occurs in the form of granules resembling starch, in the infusorian, *Euglena viridis*.)

(8. **Cellulose** occurs in the cell-walls of all plants (in the exo-skeleton of arthropoda, and the skin of snakes); soluble only in ammonio-cupric oxide; rendered blue by sulphuric acid and iodine. Boiled with dilute sulphuric acid, it yields dextrin and glucose. Concentrated nitric acid mixed with sulphuric acid changes it (cotton) into nitro-cellulose (gun-cotton) $C_6H_7(NO_2)_3O_5$, which dissolves in a mixture of ether and alcohol and forms **collodion**.)

(9. **Tunicin** is a substance resembling cellulose, and occurs in the integument of the Tunicata or Ascidians.)

IV. Division.—This contains the carbohydrates which do not ferment.

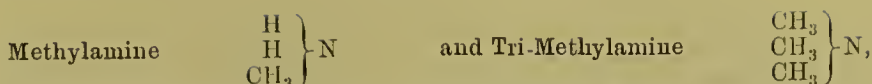
1. **Inosit**— $C_6H_{12}O_6$ —(phaseo-mannit, muscle-sugar) occurs in muscle (*Scherer*), lung, liver, spleen, kidney, brain of ox, human kidney; pathologically in urine and the fluid of echinococcus. In the vegetable kingdom, in beans (leguminosæ), and the juice of the grape. It is an isomer of grape-sugar; optically it is inactive, crystallises in warts with 2 molecules of water, in long monoclinic crystals; it has a sweet taste, is insoluble in water, does not give Trommer's reaction, is capable of undergoing only the saccharic acid fermentation. (Nearly allied are **Sorbin**, from sorbic acid—**Scyllit**, from the intestines of the hag-fish and skate—and **Encalin**, arising from the fermentation of melitose.) [Some authors however include these with the glucoses.]

[**Glycuronic acid**, $C_6H_{10}O_7$, seems to be related to the carbohydrates. It occurs in the urine as a potassium salt ($C_6H_9O_7K$), and is found in large quantity in the urine after the administration of chloral, chloroform, butylchloral, &c. It reduces alkaline solutions of copper, e.g., Fehling's solution, and is apt, therefore, to be mistaken for dextrose (§ 262). It, however, does not undergo the alcoholic fermentation as dextrose does.]

IV. Derivatives of Ammonia and their Compounds.

The **ammonia derivatives** are obtained from the proteids, and are decomposition-products of their metabolism.

(1) **Amines**, i.e. compound ammonias which can be obtained from ammonia (NH_3) or from ammonium-hydroxide ($NH_4 - OH$), by replacing one or all the atoms of H by groups of carbohydrates (alcohol radicals). The amine derived from one molecule of ammonia is called **monamine**. We are only acquainted with



as decomposition-products of cholin (neurin) and of kreatin. Neurin occurs in lecithin in a very complex combination (see Lecithin, p. 474, and also § 23).

(2) **Amides**, *i.e.* derivatives of acids which have exchanged the hydroxyl (HO) of the acids for NH_2 (Amidogen). **Urea**, $\text{CO}(\text{NH}_2)_2$, the biamid of CO_2 , is the chief end-product of the metabolism of the nitrogenous constituents of our bodies (see *Urine*, § 256). Carbon dioxide containing water = $\text{CO}(\text{OH})_2$, where both OH are replaced by NH_2 —thus we get $\text{CO}(\text{NH}_2)_2$, urea.

(3) **Amido-acids**, *i.e.*, nitrogenous compounds, which show partly the character of an acid and partly that of a weak base, in which the atoms of H of the acid-radical are replaced by NH_2 , or by the substituted ammonia groups.

(a) **Glycin** (or amido-acetic acid, glycocoll, gelatin-sugar, § 177, 2) is formed by boiling gelatin with dilute sulphuric acid. It has a sweet taste (gelatin-sugar), behaves as a weak acid, but also unites with acids as an amine-base. It occurs as glycin + benzoic acid = hippuric acid, in urine (§ 260 and also as glycin + cholalic acid = glycocholic acid in bile (§ 177). (b) **Leucin**—(§ 170) = amido-caproic acid. (c) **Serin**—(= ? amido-lactic acid) obtained from silk-gelatin. (d) **Aspartic acid**—(amido-succinic acid); and (e) **Glutamic acid**, obtained by the splitting up of proteids (§ 170). Other amido-acids are—(f) **Cystin** = amido-lactic acid, in which O is replaced by S (§ 268). (g) **Taurin**—(§ 177), amido-ethyl-sulphuric acid occurs (except in certain glands) chiefly in combination with cholalic acid, as taurocholic acid in bile. **Tyrosin** (para-hydro-oxyphenyl-amido-propionic acid), an amido-acid of unknown constitution, occurs along with leucin during pancreatic digestion (§ 170), is a decomposition-product of proteids, and occurs plentifully in the urine in acute yellow atrophy of the liver (§ 269).

To the amido-acids are related—(a) **Kreatin** in muscle, brain, blood, urine, regarded as methyl-uramido-acetic acid ($\text{C}_4\text{H}_9\text{N}_3\text{O}_2$). It has been prepared artificially. When boiled with baryta-water, it takes up H_2O , and splits into urea—and (b) **Sarkosin** ($\text{C}_3\text{H}_7\text{NO}_2$), methyl-amido-acetic acid. When boiled with water, or heated with strong acids, in the presence of putrefying substances, kreatin gives off water, and is changed into kreatinin ($\text{C}_4\text{H}_7\text{N}_3\text{O}$). This strong base can be recharged by alkalis into kreatin.

(4) **Ammonia Derivatives of Unknown Constitution**.—**Uric acid** (§ 258); **allantoin** (§ 260), is formed by the oxidation of uric acid by means of potassium permanganate; **cyanuric acid** in dog's urine; **inosinic acid** in muscle; **guanin** in traces in the liver and pancreas, in guano, the excrements of spiders, in the skin of amphibia and reptiles, in the silver sheen of many fishes (*A. Ewald and Krukenberg*); by oxidation it yields urea (p. 439); **hypoxanthin** or **sarkin** occurs along with **xanthin** in many organs and in urine. Kossel prepared hypoxanthin from nuclein by prolonged boiling of the latter. It may be obtained from fibrin by putrefaction, by gastric and pancreatic digestion, and by dilute acids (*Salomon, H. Krause, Chittenden*); **xanthin** is prepared by oxidation from hypoxanthin. It occurs very rarely in the form of a urinary calculus. **Paraxanthin** in urine, and a similar body **carnin** in flesh (§ 233). [**Adenin** ($\text{C}_5\text{H}_5\text{N}_5$), discovered by Kossel in the pancreas, yeast, and tea-leaves, has also been isolated from the spleen, lymphatic glands, and kidney; it appears to be present in all highly cellular animal and vegetable tissues. Like the allied bases, xanthin and guanin, it is a derivative of the nuclein of the nuclei.]

Aromatic Substances.

1. **Monatomic phenols**—(a) **Phenol** (hydroxyl of benzol) in the intestine (§ 180). Phenyl-sulphuric acid in urine (§ 262). (b) **Kresol**, in the form of *orthokresol* and *parakresol*, united with sulphuric acid, occur in urine (§ 262). 2. **Diatomic phenols**—(a) **pyrokatechin** united with sulphuric acid in urine (§ 262). 3. **Aromatic oxyacids**—(a) **Hydroparacumaric acid**; (b) **Paraoxyphenylacetic acid** in urine (§ 262). 4. **Indol** and **skatol** in the intestine (§ 184), conjoined with sulphuric acid in urine (§ 262). Skatol has been formed artificially by distilling strychnia with lime (*Stoehr*).

253. HISTORICAL.—According to Aristotle, the organism requires food for three purposes—for growth, for the production of heat, and to compensate for the loss of the bodily excreta. The formation of heat takes place in the heart by a process of concoction, the heat so formed being distributed to all parts of the body by means of the blood, while the respiration is regarded as an act whereby the body is cooled. Galen accepted this view in a somewhat modified form; according to him, the metabolic processes may be compared to the processes going on in a lamp; the blood represents the oil; the heart, the wick; the lungs, the fanning apparatus. According to the view of the iatrochemical school (*van Helmont*), the metabolic processes of the body are fermentations, whereby the food is mixed with the juices of the body. Since the middle of the seventeenth century (*Boyle*), the knowledge of the metabolic processes has followed the development of chemistry. A. v. Haller regarded heat as due to chemical processes—the food continually supplying the waste which is excreted from the body. After the discovery of oxygen (1774, by Priestley and Scheele), Lavoisier formulated the theory of combustion in the

lungs, whereby carbonic acid and water were formed. Mitscherlich compared the decomposition-processes in the living body with putrefactive processes. Magendie was the first to emphasise the difference between nitrogenous and non-nitrogenous foods, and he showed that the latter alone were not able to support life. Even gelatin alone is not sufficient for this purpose. The greatest advance in the theory of nutrition was made by J. v. Liebig, who laid the foundation of our present knowledge of this subject. According to Liebig, foods may be divided into two classes, viz., the "**plastic**," suitable for the construction of the organism, and the "**respiratory**" for the maintenance of the temperature; to the former class he referred the albuminates or proteids; to the latter, the non-nitrogenous carbohydrates and fats (p. 440). Amongst recent observers, the Munich School, as represented by v. Bischoff, v. Pettenkofer, and v. Voit, has done most to give us an exact knowledge of this department of physiology.

The Secretion of Urine.

[**Elimination of Waste Products.**—We have seen that the tissues are nourished by the lymph, which contains the chemical compounds—proteids, carbohydrates, fats, salts, and gases—necessary for nourishing the tissues. As a result of the activity of the tissues, certain waste-products are formed which are removed from the tissues either by passing directly into the lymph-stream, by which they ultimately enter the blood,—or certain of these waste-products pass into the venous blood. In any case, the blood contains these **waste-products** and they must be got rid of, for if they accumulate to any great extent in the blood they injure the tissues. These matters are eliminated from the blood by various organs—called **excretory organs**—while the substances so excreted are called **excretions**.]

[A complete acquaintance with all the facts of the case would enable us to trace step by step the various changes which the neutral substances undergo before they become effete products, but our acquaintance with what goes on in the economy does not enable us to do so completely. Speaking broadly, however, the chief waste-products are urea, and certain closely allied nitrogenous bodies, carbon dioxide, salts, and water. These substances leave the body by one or other of three main channels. Much of the water, urea, and allied bodies, and the greater portion of the salts, are eliminated in the urine by the kidneys. These organs are of special importance, as nearly all the waste bodies containing nitrogen are eliminated in the urine. Through the skin—in the sweat—is eliminated a large but variable quantity of water, a very small amount of salts, and a little carbon dioxide. The lungs serve as the chief channel for the elimination of carbon dioxide and a considerable quantity of water in the form of aqueous vapour.

[Besides these main channels the liver excretes substances in the bile, some of which are ultimately discharged, perhaps in a somewhat altered form, in the fæces. As we have seen, some of the undigested food is excreted by the bowel and along with it certain residues derived from the secretions poured into the intestinal canal.]

254. STRUCTURE OF THE KIDNEY.—[**Capsule.**—The kidney is a compound tubular gland, and is invested by a thin, tough, fibrous capsule, easily stripped off from the substance of the organ, to which it is attached by fine processes of connective-tissue and blood-vessels.]

[**Naked Eye Appearances.**—On dividing the kidney longitudinally from the hilum to its outer border, and examining the cut surface with the naked eye, we observe the **parenchyma** of the kidney, consisting of an outer **cortical** and an inner **medullary**, or pyramidal portion, the latter composed of about twelve conical papillæ, or **pyramids of Malpighi**, with their apices directed towards and embraced by the calices of the pelvis of the kidney (fig. 296). The medullary portion is

further subdivided into the **boundary layer** of Ludwig and the **papillary portion**. According to Klein, the relative proportions of these three parts are—cortex, 3·5; boundary layer, 2·5, and papillary portion, 4. The **cortex** has a light brown colour, and when torn presents a slightly granular aspect, with radiating lines running at regular distances. The granules are due to the presence of the Malpighian corpuscles, and the striae to the medullary rays. The boundary zone is

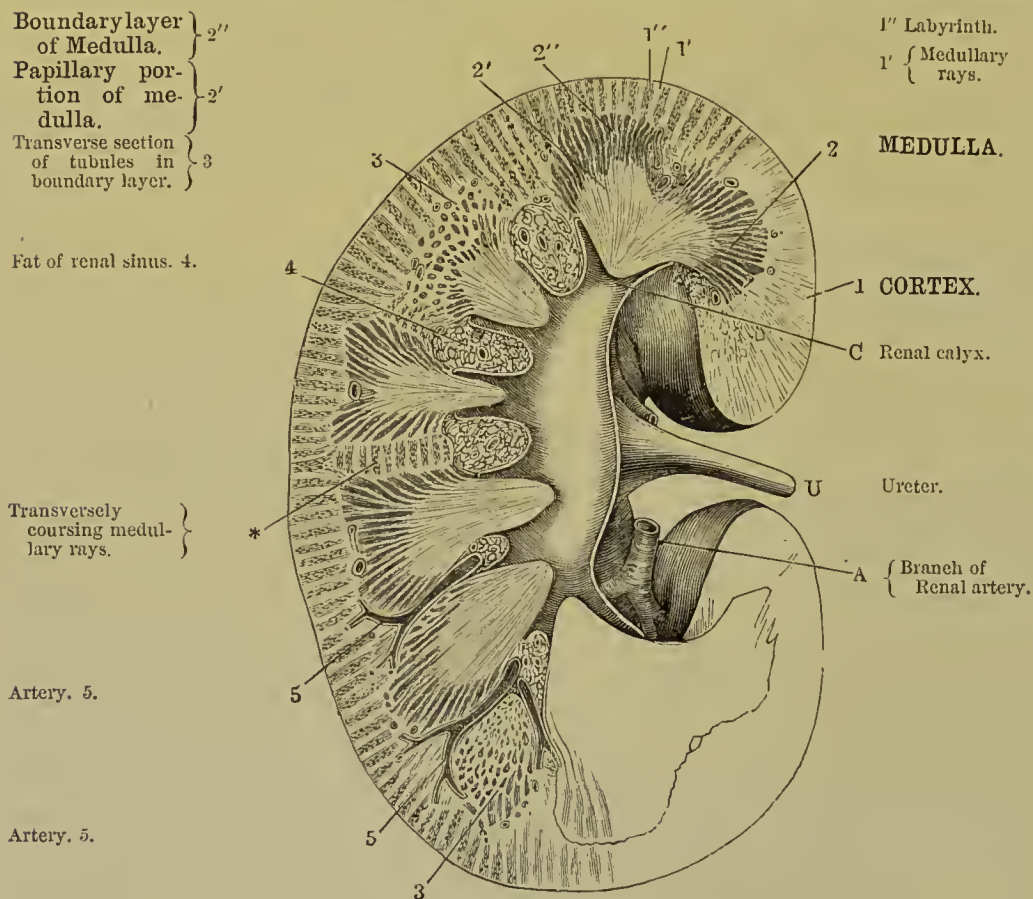


Fig. 296.

Longitudinal section through the kidney (*Tyson, after Henle*).

darker, and often purplish in colour. It is striated with clear and red lines alternating with opaque ones, the former being blood-vessels and the latter uriniferous tubules. The papillary zone is nearly white and uniformly striated, the striae converging to the apex of the pyramid. The **medulla** is much denser and less friable than the cortex, owing to the presence of a large amount of connective-tissue between the tubules. The bundles of straight tubes of the medulla may be traced at regular intervals running outwards into the cortex, constituting **medullary rays**, which become smaller as they pass outwards in the cortical zone, so that they are conical and form the **pyramids of Ferrein** (fig. 298, PF). The portion of the cortex lying between the medullary rays is known as the **labyrinth**, from the complicated arrangement of its tubules.]

[**Size, Weight of Kidney.**—The adult kidney is about 11 centimetres (4·4 inches) in length, 5 centimetres (2 inches) wide, and 3 centimetres (1 inch) in thickness. It weighs in the male 113·5 to 170 grms. (4 to 6 oz.), in the female 113·5 to 156 grms. (4 to 5½ oz.). The width of the cortex is usually 5 to 6 millimetres (¼ to ¼ inch).]

I. The **uriniferous tubules** all arise within the labyrinth of the cortex by means of a globular enlargement, 200 to 300 μ [$\frac{1}{100}$ to $\frac{1}{125}$ inch] in diameter, called **Bowman's capsule** (figs. 298, 299). After pursuing a complicated course, altering their direction, diameter, and structure, and being joined by other tubules, they ultimately form large collecting tubes, which terminate by minute apertures, visible with the aid of a hand-lens, on the apices of the papillæ projecting into the calices of the kidney. Each urinary tubule is composed of a homogeneous **membrana propria**, lined by a single layer of epithelial cells, so as to leave a lumen for the passage of the urine from the Malpighian corpuscles to the pelvis of the kidney. The diameter and direction of the tubules vary, and the epithelium differs in its characters at different parts of the tube, while the lumen also undergoes alterations in its diameter.

Course and Structure of the Tubules.

—In the labyrinth of the cortex, tubules arise in the spherical enlargement known as **Bowman's capsule** (fig. 298, 1), which invests (in the manner presently to be described) the tuft of capillary blood-vessels called a **glomerulus** or **Malpighian corpuscle**. By means of a short and narrow neck (2) the capsule becomes continuous with a convoluted tubule, X in fig. 299. This tubule is of considerable length, forming many windings in the cortex (fig. 298, 3); the first part of it is 45 μ wide, constituting the **proximal** or **first convoluted tubule**. It becomes continuous with a **spiral tubule** of Sehachowa (4), which lies in a medullary ray where it pursues a slightly wavy or spiral course. On the boundary line between the cortical

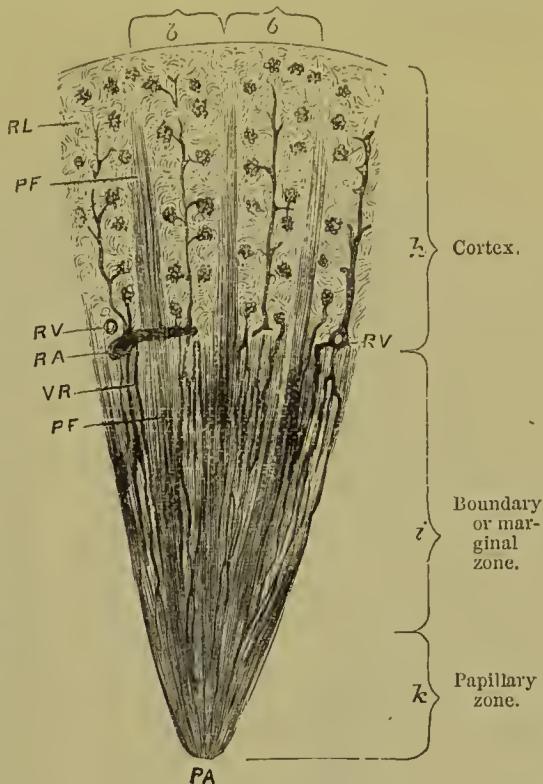


Fig. 297.

Longitudinal section of a Malpighian pyramid. PF, pyramids of Ferrein; RA, branch of renal artery; RV, lumen of a renal vein receiving an interlobular vein; VR, vasa recta; PA, apex of a renal papilla; b, b, embrace the bases of the renal lobules.

and boundary zone, the spiral tubule suddenly becomes smaller and passes into the **descending portion** of **Henle's loop** (5), which is 14 μ in breadth, and is continued downwards through the boundary zone into the medulla, where it forms the narrow **loop of Henle** (6) which runs backwards in the medullary part to the boundary zone. Here it becomes wider (20–26 μ), and as it continues its undulating course, it enters a medullary ray, where it constitutes the **ascending looped tube** (7), which becomes narrower in the cortex. Leaving the medullary ray again, it passes into the labyrinth, where it forms a tube with irregular angular outlines—the **irregular tubule** (10), which is continuous with (fig. 299, n, n) the **second** or **distal convoluted tubule** (11), which resembles the proximal tubule of the same name. Its diameter is 40 μ . A short, narrow, wavy **junctional** or **curved collecting tubule** (12) connects the latter with one of the **straight collecting tubes** (13) of a medullary ray. As the collecting tubule proceeds through the boundary zone, it receives numerous junctional tubes, and when it reaches the boundary zone, it forms one of the **collecting tubes** (fig. 299, O),

which unite with one another at acute angles to form the larger straight **excretory tubes** or ducts of Bellini (15), which open on the summit of the Malpighian pyramids into a calyx of the pelvis of the kidney. In the cortex the collecting tubules are $45\ \mu$ in diameter, but where they have formed an excretory tube (O),

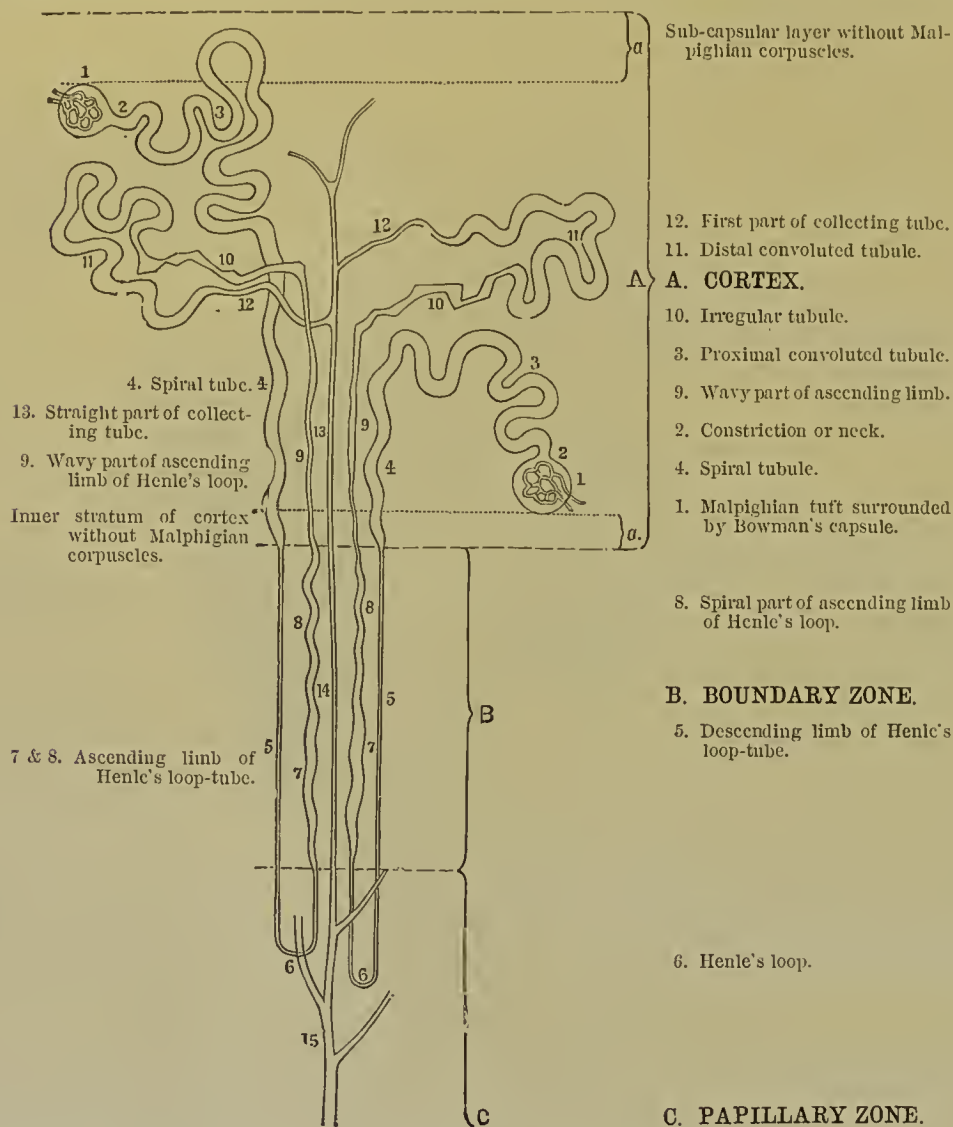


Fig. 298.

Diagram of the course of two uriniferous tubules (*Klein and Noble-Smith*).

their diameter is 200 to $300\ \mu$; 24 to 80 of these tubes open on the apex of each of the 12 to 15 Malpighian pyramids. In the lowest and broadest part, the membrana propria is strengthened by the presence of a thick supporting framework of connective-tissue.

Structure of the Tubules.—[Below the neck, the tubules are lined everywhere by a single layer of nucleated epithelium.] **Bowman's capsule**, which is about $\frac{1}{250}$ inch in diameter (fig. 300, II), consists of a homogeneous basement membrane lined internally by a single continuous layer of flattened cells (*k*). According to Roth, the basement membrane itself is composed of endothelial cells. [In the foetus the lining cells are more polyhedral.] Within the capsule lies the

glomerulus or tuft of blood-vessels. The cells lining the capsule are reflected over and between the lobules of which the glomerulus consists. The glomerulus may not completely fill the capsule, so that, according to the activity of the kidney, there may be a larger or smaller space between the glomerulus and the capsule into which the filtered urine passes. The **neck** is lined by cubical cells. These cells, in some animals, *e.g.*, the rabbit, sheep, mouse, and frog, are ciliated.

[The **proximal convoluted tubule** is lined by characteristic epithelium. The cells, which are short or polyhedral, contain a turbid or cloudy protoplasm (fig. 300, III, 1 and 2), which not unfrequently contains oil-globules, and they form a single layer. Each cell consists of two parts; the inner, containing the spherical nucleus, is next the lumen, and granular (III, 2, *g*), while the outer part, next the membrana propria, appears fibrillated, or "rodged," from the presence of rods or fibrils placed vertically to the basement-membrane (fig. 301). These appear like the hairs of a brush pressed upon a plate of glass (III, 2). The cells are not easily separated from each other, as neighbouring cells interlock by means of the branched ridges on their surfaces (III, 1) — (*Heidenhain, Schachnowa*). The lumen is well defined, but its size seems to depend upon the state of imbibition of the cells bounding it.

The **spiral tubule** has similar epithelium and a corresponding lumen, although the epithelium becomes lower and somewhat altered in its characters at the lower part of the tube.

The **descending limb of Henle's loop**, and the **loop** itself with a relatively wide

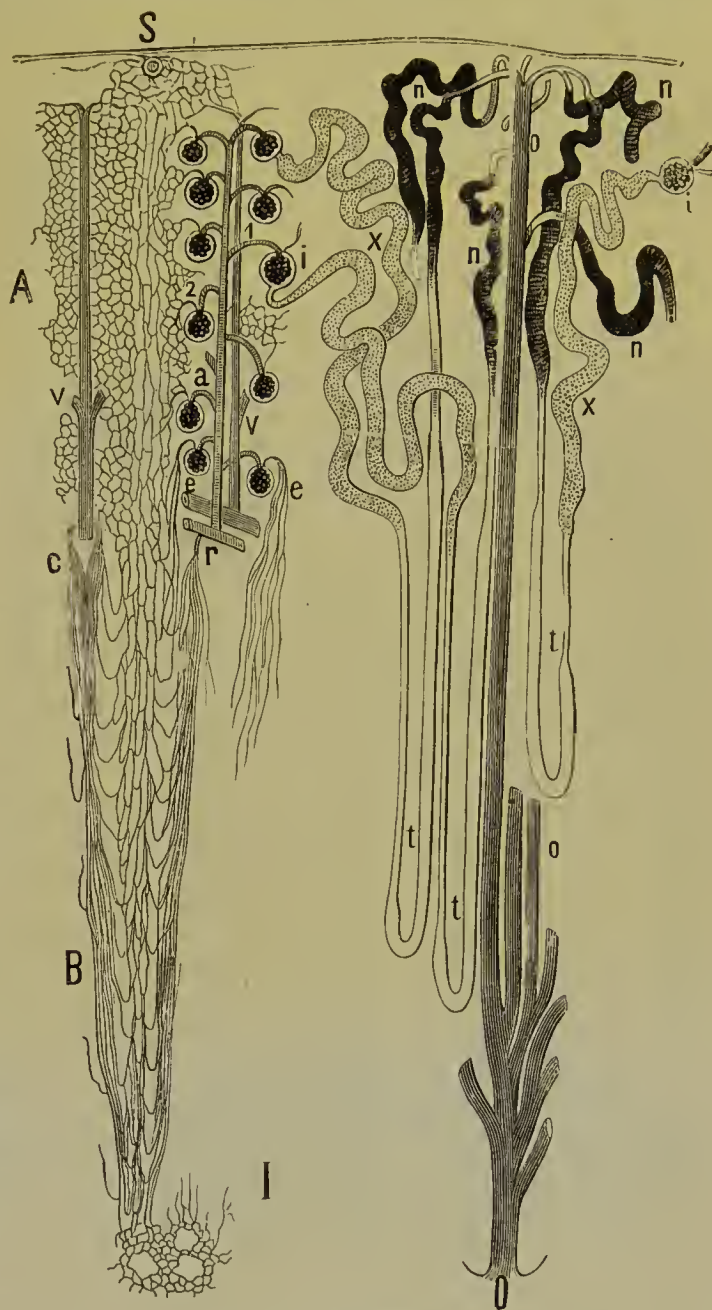


Fig. 299.

Blood-vessels and uriniferous tubules of the kidney (semi-diagrammatic); A, capillaries of the cortex, B, of the medulla; a, interlobular artery; 1, vas afferens; 2, vas efferens; r, e, vasa recta; c, venae rectae; v, v, interlobular vein; S, origin of a vena stellata; i, i, Bowman's capsule and glomerulus; X, X, convoluted tubules; t, t, Henle's loop; n, n, junctional pieces; o, o, collecting tubes; O, excretory tube.

lumen, are bounded by clear, flattened, epithelial cells, with a bulging nucleus (IV, S); the cells lying on one side of the tube being so placed that the bulging part of the bodies of the cells is opposite the thin part of the cells on the opposite side of the tube. [These tubes might be mistaken for blood-capillaries, but in addition to their squamous lining, they have a basement-membrane, which capillaries

have not.] In the **ascending limb**, the lumen is relatively wide, while its epithelium agrees generally with that in the convoluted tubule, excepting that the "rods" are shorter. Sometimes the cells are arranged in an "imbricate" manner.

In the **irregular tubule**, which has a very small lumen, the polyhedral cells lining it contain oval nuclei, and are shorter than those of the convoluted tubules. The cells, again, are very irregular in size, while their "rodlike" character is much coarser and more defined (fig. 303).

The **distal convoluted tubule** closely resembles

in its structure the proximal convoluted tubule, and is lined by similar cells. The *curved collecting*, or **junctional tubule**, although narrow, has a relatively wide lumen, as it is lined by clear, somewhat flattened cells.

The **collecting tubes** have a distinct lumen and are lined by *clear*, somewhat irregular, cubical cells (fig. 300, V), which in the larger *excretory* tubes are distinctly columnar (VI). The basement-membrane is said to be absent in the larger

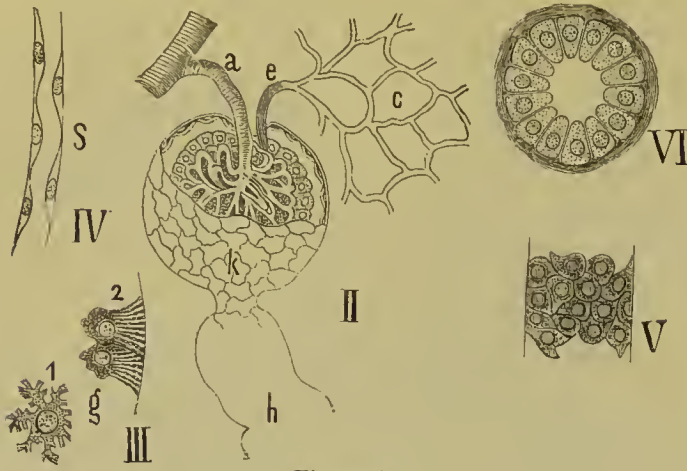


Fig. 300.

II, Bowman's capsule and glomerulus. *a*, vas afferens; *e*, vas efferens; *c*, capillary network of the cortex; *k*, endothelium of the capsule; *h*, origin of a convoluted tubule. III, "rodlike" cells from a convoluted tubule—2, seen from the side, with *g*, inner granular zone; 1, from the surface. IV, cells lining Henle's looped tubule. V, cells of a collecting tube. VI, section of an excretory tube.



Fig. 301.

Convoluted tubule (after ammonium chromate) showing "rodlike" epithelium.



Fig. 302.

Epithelium of an irregular tubule of the kidney of a dog.

tubes. [Klein describes a thin, delicate, nucleated centro-tubular membrane lining the surface of the epithelium next the lumen.]

II. The Blood-Vessels.—[Considering the size of the kidney it is most abundantly supplied with blood.]—The **renal artery** (fig. 306) divides into four or five branches, which pass into the kidney at the hilum. These branches, surrounded by connective-tissue continuous with that of the capsule, continue to divide, and pass between the papillae, to reach the bases of the pyramids on the limits between the cortical and boundary zones where they form incomplete arches. From these horizontal trunks, the **interlobular** or **radiate arteries** (fig.

299, *a*) run vertically and singly into the cortex, between each two medullary rays, and in their course they give off on all sides the short undivided **vasa afferentia** (1), each of which enters a Malpighian capsule at the opposite pole from which the urinary tubule is given off. Within the capsule each afferent artery breaks up into capillaries arranged in lobules and supported by connective-tissue, the whole forming a tuft of capillary blood-vessels, or a **glomerulus**. Each glomerulus is covered on its surface, directed towards the wall of the capsule by a layer of flat, nucleated, epithelial cells (fig. 300, II), which also dip down between the capillaries. A vein, the **vas efferens** (2), which is always smaller than the afferent arteriole, proceeds from the centre of the glomerulus, and leaves the capsule close to the point at which the afferent vessel enters it (fig. 300, II). In their structure and distribution all the efferent vessels resemble arteries, as they divide into branches to form a dense, narrow-meshed, **capillary network** (fig. 299, A, and fig. 300, II, *c*), which ramifies over and between the convoluted tubules. The meshes are elongated around the tubules of the medullary rays, and more polygonal around the convoluted tubules (fig. 299). Some of the lowest efferent vessels split up into **vasa recta**, which run towards the medulla. The interlobular arteries become smaller as they pass towards the surface of the kidney, and some of their terminal capillaries communicate with the capillaries of the external capsule itself. Venous trunks proceed from the capillary network, to terminate in the **interlobular veins** (V), which begin close under the capsule by venous radicles arranged in a stellate manner (constituting the stellulæ Verheyneii, or **venæ stellatæ**), and accompanying the corresponding artery to the limit between the cortex and boundary zone, where they communicate with the large venous trunks in that situation. [The subcapsular layer of the cortex, and a thin layer next the boundary zone (fig. 298, *a*, *a*), are devoid of Malpighian corpuscles.]

The **blood-vessels of the medulla** arise from the **vasa recta** (fig. 299, *r*), which begin on the limit of the cortex and medulla, either as single, direct, muscular branches (*r*) of the large arterial trunks, or from those efferent vessels (*e*) which lie next to the medulla. The latter are said to be devoid of muscle. According to Huschke, a few vasa recta are formed by the union of the capillaries of the medullary rays. All the vasa recta enter the boundary layer, where they split up into a leash or pencil of small arterioles, which pass between the straight tubules towards the pelvis, and form in their course a capillary network with elongated meshes. From these capillaries there arise venous radicles, which, as they proceed towards the limit between the cortex and medulla, form the **venæ rectæ** (*c*), and open into the concave side of the venous trunks in this region. At the apex of the papillæ, the capillaries of the medulla form connections with the rosette-like capillaries surrounding the excretory ducts (at I).

The **circulation through the vasa recta** is most important. The cortical system of blood-vessels communicates with the medullary, but as most of the vasa recta are derived from the same vessel as the interlobular arteries, it is evident that they may form a side stream through which much of the blood may pass without traversing the vessels of the cortex. Very probably the "short-cut" is useful in congestions of the kidney. The amount of distention of these vessels also will influence the size of the tubules lying between them. There are two other channels by which blood can pass through the renal arteries without traversing the glomeruli—(1) The anastomoses between the terminal twigs of the renal artery and the subcapsular venous plexus; (2) small branches given off, either by the interlobular arteries or by the afferent vessels before entering the glomeruli (*Brunton*).]

The **blood-vessels of the external capsule** are derived partly from the terminal twigs of the interlobular arteries, partly from branches of the supra-renal,

phrenic, and lumbar arteries, which anastomose with each other. The capillary network has simple meshes. The venous radicles pass partly into the venæ stellatæ, and partly into the veins of the same name as the arteries. The connection of the area of the renal artery with the other arteries of the capsule explains why, after ligature of the renal artery within the kidney, the blood still circulates in the external capsule (*C. Ludwig, M. Herrman*); in fact, these blood-vessels still supply the kidney with a small amount of blood, which may suffice to permit a slight secretion of urine to take place (*Litten, Pautynski*).

III. The **lymphatics** form a wide-meshed plexus in the capsule of the kidney, while under it they form large spaces (*Heidenhain*). In the parenchyma of the kidney, the lymphatics are said to be represented by large slits devoid of a wall in the tissues, and are more numerous around the convoluted than the straight tubules. The slits pass to the surface of the kidney, and expand under the capsule. When the lymphatics are greatly distended, they tend to compress the uriniferous tubules and the blood-vessels (*C. Ludwig and Zawarykin*). According to Ryndowsky, the uriniferous tubules are surrounded by true lymphatics with an endothelial lining, and they even penetrate into the capsule of Bowman along with the vas afferens. [The large blood-vessels are also surrounded by lymphatics.] Large lymphatics, provided with valves, pass out of the kidneys at the hilum, while others emerge through the capsule; both sets are connected with the lymph-spaces of the capsule of the kidney (*A. Budge*).

IV. The **nerves** form small trunks provided with **ganglia**, and accompany the blood-vessels. [They are derived from the renal plexus and the lesser splanchnic nerve.] The nerves forming the **renal plexus** are derived chiefly from the solar

plexus. As the right vagus and great and lesser splanchnics join the solar plexus, it is probable that branches of these nerves enter the kidney by way of the renal plexus. The splanchnics, however, send branches direct to the renal plexus, and the left vagus sends some fibres to the left kidney. In the dog the 11th, 12th, and 13th dorsal spinal nerves, and perhaps some of the upper lumbar nerves, send branches into the kidney *viâ* the renal plexus (§ 276). They contain medullated and non-medullated fibres, and the latter have been traced by W. Krause as far as the apices of the papillæ. Their mode of termination is unknown. *Physiologically*,

we are certain that they contain both *vaso-constrictor*, *vaso-dilator*, and *sensory* fibres; perhaps there may be also secretory fibres [although we have no evidence of the termination of nerve-fibres in the epithelium of the tubules].

V. The **connective-tissue**, or interlobular stroma, forms in the papillæ, especially at their apices, fibrous, concentric layers of considerable thickness between the excretory tubules (fig. 303). Further outwards, the fibrillar character becomes less

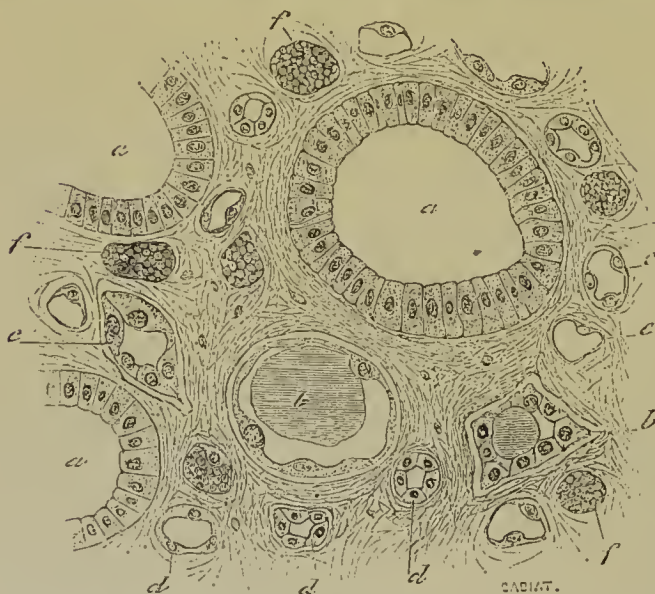


Fig. 303.

Transverse section of apex of Malpighian pyramid. *a*, large collecting tubes; *b*, *c*, *d*, tubules of Henle; *e*, *f*, blood-vessels.

distinct, while at the same time branched connective-tissue corpuscles occur in greater numbers. In the cortex, the interstitial stroma consists almost entirely of branched corpuscles, which anastomose with each other. [There is also a small quantity of delicate fibrous tissue around Bowman's capsule, and along the course of the arteries. The connective-tissue often plays an important rôle in pathological conditions of the kidney, as interstitial nephritis.] The outer layers of the capsule of the kidney are composed of dense bundles of fibrous tissue, while the deeper layers are more loose, and send processes into the cortical layers. The capsule is easily stripped off. None of the secretory substance is removed with it. The fat surrounding the kidney is united to the latter partly by blood-vessels and partly by bands of connective tissue.

VI. **Smooth Muscle** is present (1) as a sphincter-like layer round the apex of each papilla (*Henle*); (2) as a wide-meshed thin plexus on the surface of the kidney just under the capsule; (3) as fine fibres derived from the pelvis of the kidney and which pass along with the blood-vessels into the pyramids (*Jardet*). (4) *Kostjurin* found in the dog in the boundary zone between the cortex and medulla a layer of muscle which sends prolongations into both zones.

[**Development of a Malpighian Capsule.**—The upper end of the urinary tubule is dilated and closed, and into it there grows a tuft of blood-vessels (*a*) pushing one layer of the tube (*b*) before it, hence the capillaries become invested by it, just as an organ is surrounded by a serous sac, so that one layer—the reflected one (*b*)—of the tubule is closely applied to the blood-vessels, while the other (*c*) lies loosely over it with a space between the two (fig. 304).]



Fig. 304.



Fig. 305.



Fig. 306.

255. THE URINE.—Physical Characters.—A knowledge of the composition of this secretion is of the greatest value to the physician and surgeon.

1. The **quantity** of urine passed by an adult man in twenty-four hours is between 1000 and 1500 cubic centimetres, or about 50 oz., and in the female 900 to 1200 c.c. The minimum is secreted between 2 to 4 A.M., and the maximum between 2 to 4 P.M. (*Weigelin*).

The **amount** is diminished by profuse sweating, diarrhoea, thirst, non-nitrogenous food, diminution of the general blood-pressure, after severe hæmorrhage, and in some diseases of the kidneys. The minimum, which may be normal, is 400 to 500 c.c. It is increased by increase of the general blood-pressure, or of the pressure within the area of the renal artery, by copious drinking, contraction of the cutaneous vessels through the action of cold, the passage of a large amount of soluble substances (urea, salts, and sugar) into the urine, a large amount of nitrogenous food, as well as by various drugs, such as digitalis, alcohol, squills. After taking fluids charged with CO₂, the amount of urine is increased during the following hours (*Quinke*).

The secretion is influenced directly by the nervous system, as in the sudden polyuria following nervous excitement, such as hysteria, [when the person usually passes a large amount of very pale-coloured urine]; after an epileptic attack, and also after pleasurable excitement (*Bencke*).

Fig. 304.—Development of a glomerulus and Malpighian capsule. *a*, capillary; *b*, visceral, *c*, parietal layer of capsule.

Fig. 305.—Graduated cylinder and flask for measuring the amount of urine.

Fig. 306.—Urinometer.

We may have polyuria unaccompanied by the presence of sugar in the urine, which follows injury to a certain part of the floor of the fourth ventricle (*Cl. Bernard*). The urine is measured in tall graduated cylindrical vessels (fig. 305). [In estimating the quantity of urine passed, the patient must, of course, be directed always to empty his bladder at a particular hour, and collect the urine passed during the next twenty-four hours.]

[**Comparative.**—In *man* 60 per cent. of the water eliminated from the body is given off by the kidneys, and 40 by the lungs and skin. In *herbivora* 30 per cent. of the water is eliminated by the kidneys and 70 by the lungs and skin, while in *carnivora* the proportions are 70 by the urine and 30 by the lungs and skin (*Munk*).]

2. The **specific gravity** varies, as a mean, between 1015 and 1025; the minimum, after copious draughts of water, may be 1002; while the maximum, after profuse perspiration and great thirst, may be 1040. The mean specific gravity is about 1020. In newly-born children, the specific gravity falls very considerably during the first three days, which is due to the amount of food taken (*Martin and Ruge*). [The specific gravity of the urine in **infants** is about 1003 to 1006.] A healthy adult excretes about 70 grms. [$2\frac{1}{2}$ oz.] daily of solids by the urine, or about 1 grm. of solids per 1 kilo. of body weight.

The **specific gravity** is estimated by means of a urinometer (fig. 306), the urine being at the temperature of 16° C. [The **urinometer**, when placed in distilled water, ought to float at the mark 0° or zero, which is conventionally spoken of as 1000. Place the urine to be tested in a tall cylindrical glass, of such width that the urinometer, when placed in it, may float freely and not touch the sides. Take care that no air-bubbles adhere to the instrument. When reading off the mark on the stem, raise the vessel to the eye and bring the eye on a level with the surface of the water, noting the number which corresponds to this. This rule is adopted, because the water rises on the stem in virtue of capillarity. It is essential that a sample of the **mixed urine** of the twenty-four hours be used for ascertaining the mean specific gravity.]

Christison's Formula.—To estimate the amount of solids in the urine. This may be done approximately by means of the formula of Trapp or Haeser, or, as it is called in this country, "Christison's Formula," viz., "Multiply the two last figures of a specific gravity expressed in four figures by 2·33" (*Christison and Haeser*), or by 2 (*Trapp*), or 2·2 (*Loebisch*). This gives the amount of solids in every 1000 parts. [Suppose a person passes 1200 c.c. urine in twenty-four hours, and the specific gravity is 1022, then

$$22 \times 2 \cdot 33 = 51 \cdot 26 \text{ grms. in 1000 c.c.}$$

To ascertain the amount in 1200 c.c.

$$1000 : 1200 :: 51 \cdot 26 : x = \frac{51 \cdot 26 \times 1200}{1000} = 61 \cdot 51 \text{ grms.}]$$

Direct Estimation of Solids.—Place 15 c.c. of urine in a capsule of known weight, and evaporate it to dryness over a water-bath; afterwards completely dry the residue in an air-bath at 100° C., and then cool it over concentrated sulphuric acid. During the process, a small amount of urea is decomposed, so that the value obtained is slightly too small. Of course the specific gravity varies with the amount of water in the urine. The *most concentrated* (highest specific gravity) urine is the morning urine (*Urina noctis*), especially after being retained in the bladder, e.g., in prolonged sleep a certain amount of water is absorbed, so that the urine becomes more concentrated. The most dilute urine is secreted after copious drinking (*Urina potus*). Under **pathological conditions**, as in diabetes mellitus (§ 175), the urine is, at the same time, very copious (as much as 10,000 c.c.), and very concentrated, so that the specific gravity varies from 1030 to 1060, [due to the presence of a large amount of grape-sugar]. In fever the urine is concentrated and small in amount. In polyuria, due to certain nervous conditions, the urine is very dilute and copious, while the specific gravity may be as low as 1001.

3. The **colour** of the urine depends on the colouring-matters present in it, and varies greatly, but the differences in colour are due chiefly to variations in the amount of water. Normally it has a pale straw colour, but if it contains more water than usual it has a very pale tint, and in certain cases (as in the sudden polyuria occurring after an attack of hysteria) it may be as clear as water. Concentrated urine, as after meals, or the first urine passed in the morning, has a darker colour; it is a dark yellow or brownish-red; while it is usually dark coloured in fever.

Fœtal urine, and also the urine first passed after birth, are as clear and colourless as water. The admixture of various substances with the urine alters its colour. When mixed with blood according to the degree of decomposition of the hæmoglobin, the urine is red or dark brownish

red [more frequently it is *smoky*], especially if the blood comes from the kidneys and the urine is acid. When mixed with **bile pigments**, it is of a deep yellowish-brown, with an intense yellow froth; senna taken internally makes it intensely red, rhubarb brownish-yellow, and carbolic acid black. Urine undergoing the ammoniacal fermentation may present a dirty bluish appearance owing to the formation of indigo. The colour of urine is estimated by Neubauer and Vogel by means of an empirical "colour-scale."

Urine, but especially ammoniacal urine, exhibits **fluorescence**, which disappears on the addition of an acid, and reappears after the addition of an alkali.

Normal urine, after standing for several hours, deposits a fine cloud of vesical **mucus** [like delicate cotton wool]. The froth of normal urine is white, and disappears pretty rapidly, while that on an albuminous urine persists much longer. The urine not unfrequently contains some **epithelial cells** from the bladder and urethra.

[Of the **total solids** (= 65 grams) urea = about 32 grams, ehlorides = 15 grams, phosphoric acid = 2·5 grams = 49·5 grams; the remainder consists of other substances, so that about $\frac{2}{3}$ are organic and $\frac{1}{3}$ inorganic.]

[The following table gives approximately the average quantities in grams of the chief substances exereted in the urine by a healthy adult in 24 hours.

		Total Amount in Grams.	Percentage in Grams.
Water,	.	1440 - 1500	96
Solids,	.	57 - 68	4
Organic	{ Urea,	28 - 32	2·5 - 3
	{ Uric Acid,	·7	·05
	{ Hippuric acid,	·3 - 2	·015 - ·1
	{ Kreatinin,	1·7 - 2·1	·1
Inorganic	{ Sodic chloride,	15 - 20	1 - 1·25
	{ Phosphoric acid,	2·5 - 3	·16
	{ Sulphuric acid,	2 - 2·5	·15
	{ Sodium,	5 - 7	·4
	{ Magnesium,	·4	·03
	{ Potassium,	3 - 4	·25
	{ Calcium,	·3	·02]

[AMOUNTS OF THE SEVERAL URINARY CONSTITUENTS (<i>Loebisch</i>).					[AMOUNTS OF THE SEVERAL URINARY CONSTITUENTS PASSED IN 24 HOURS (<i>Parkes</i>).		
CONSTITUENTS.	Man, 28 years of age, weight, 72 kilos., observa- tions over 8 days (<i>Kerner</i>).			Mean of analyses in different individuals (<i>Vogel</i>).	CONSTITUENTS.	By an aver- age man of 66 kilos.	Per 1 kilo. of body- weight.
	In 24 hours.			In 24 hours.			
	Min.	Max.	Mean.				
	c.c.	c.c.	c.c.	c.c.		grms.	grms.
Quantity, ...	1099	2150	1491	1500	Water, ...	1500·000	23·000
Specific gravity, . . .	1015	1027	1021	1020	Total solids, ...	72·000	1·100
Water, ...	...	...	...	1440	Urea, ...	33·180	0·500
Solids, ...	...	...	...	60	Uric acid, ...	0·555	0·0084
Urea, ...	32·00	43·4	38·1	35	Hippuric acid, ...	0·400	0·0060
Uric acid, ...	0·69	1·37	0·94	0·75	Kreatinin, ...	0·910	0·0140
Sodium chloride, . . .	15·00	19·20	16·8	16·5	Pigment and other substances, ...	10·300	0·1510
Phosphoric acid, . . .	3·00	4·07	3·42	3·5	Sulphuric acid, ...	2·012	0·0305
Sulphuric acid, ...	2·26	2·84	2·48	2·0	Phosphoric acid, . . .	3·164	0·0486
Phosphorus, Calcium, .	0·25	0·51	0·38	...	Chlorine, ...	7·000 (8·12)	0·1260
Magnesium phosphate, .	0·67	1·29	0·97	...	Ammonia, ...	0·770	...
Total quantity of earthy phosphates, }	0·92	1·80	1·35	1·2	Potassium, ...	2·500	...
Ammonia, ...	0·74	1·01	0·83	0·65	Sodium, ...	11·090	...
Free acid, ...	1·74	2·20	1·95	3]	Calcium, ...	0·260	...
					Magnesium, ...	0·207	...]

4. **Consistence**.—Normal urine, like water, is a freely mobile fluid. [The temperature is about 39° C.]

Large quantities of sugar, albumin, or mucus make it less mobile; while the so-called chylous urine of warm climates may be like a white jelly.

5. The **taste** is a saline bitter, the **odour** is characteristic and aromatic.

Ammoniacal urine has the odour of ammonia. Turpentine taken internally gives rise to the odour of violets, copaiba and cubeba a strongly aromatic, and asparagus an unpleasant odour.

Valerian, assafoetida, and castoreum [but not camphor] also produce a characteristic odour. [The odour of diabetic urine is described as "sweet."]

6. The reaction of normal urine is acid, owing to the presence of acid salts, chiefly acid sodic phosphate, $[\text{NaH}_2\text{PO}_4]$ which seems to be derived from basic sodic phosphate, owing to the uric acid, hippuric acid, sulphuric acid, and CO_2 taking to themselves part of the soda, so that the phosphoric acid forms an acid salt. After a diet of flesh, acid potassic phosphate is the cause of the acidity. That the urine contains no free acid is proved by the fact that it gives no precipitate with sodic hyposulphite (*v. Voit, Huppert*). [The uric acid exists as urates, the hippuric acid also is not free, but exists as an alkaline hippurate. Brücke has proved this by congo-red, which gives a violet or inky colour with one part of free hippuric acid in 55,000 of water, but urine gives no change of colour.]

The acid reaction is increased after the use of acids, *e.g.*, hydrochloric and phosphoric, also by ammoniacal salts, which are changed within the body into nitric acid; lastly, after prolonged muscular exertion. The morning urine is strongly acid. [Sometimes under pathological conditions free fatty acids appear in the urine (lipaciduria).]

The urine becomes less acid or alkaline—(1) By the use of caustic alkalis, alkaline carbonates, or alkaline salts of the vegetable acids, the last being oxidised within the body into carbonates. (2) By the presence of calcic or magnesia carbonate. (3) By admixture with alkaline blood, or pus. (4) By removing the gastric juice through a gastric fistula (*p. 293—Maly*); further, from one to three hours after a meal. [The reaction of urine passed during digestion may be neutral, or even alkaline. This is due either to the formation of acid in the stomach (*Bence Jones*), or to a fixed alkali derived from the basic alkaline phosphates taken with the food (*W. Roberts*).] (5) The urine is rarely alkaline in anæmia, owing to a deficiency of phosphoric and sulphuric acids. [(6) The nature of the food—vegetable food makes it alkaline. (7) By profuse sweating. (8) By absorption of alkaline transudations (blood, serum).]

[Method.—The reaction of urine is tested by means of litmus paper. Normal urine turns blue litmus paper red, and does not affect red litmus. An alkaline urine makes red litmus paper blue, while a neutral urine does not alter either blue or red litmus paper.] Sometimes violet litmus paper is used, which becomes red in acid, and blue in alkaline urine.

Estimation of the Acidity.—This is done by determining the amount of caustic soda necessary to produce a neutral reaction in 100 c.c. of urine. A soda solution, containing 0.0031 gm. of soda in each c.c., is used; 1 c.c. of this solution exactly neutralises 0.0063 gm. oxalic acid. To the 100 c.c. of urine in a beaker, soda solution is added, drop by drop, from a graduated burette (*fig. 307*), until violet litmus paper becomes neither red nor blue. The number of c.c. of soda solution is now read off on the burette, and as each c.c. corresponds to 0.0063 gm. oxalic acid, we can easily calculate the amount of oxalic acid which is equivalent to the degree of acidity in 100 c.c. of urine. So that the degree of acidity of the urine is expressed by the equivalent amount of oxalic acid, which is completely neutralised by the same amount of caustic soda.]

[Urine of Mammals.—The urine of *carnivora* is pale, passing into a golden-yellow; its specific gravity is high, and its reaction strongly acid. The urine of *herbivora* is alkaline; it shows a precipitate of earthy carbonates (hence, it effervesces on the addition of an acid), and of basic earthy phosphates. During hunger, the urine presents the character of that of *carnivora*, as the animal in this case practically lives upon its own flesh and tissues.]

256. I. THE ORGANIC CONSTITUENTS OF URINE.—Urea, $\text{CO}(\text{NH}_2)_2$, the diamid of CO_2 , or carbamid, is the chief end-product of the oxidation of the nitrogenous constituents of the body (*p. 419*). Its composition is comparatively simple: 1 carbonic acid + 2 ammonia – 1 water. It crystallises in silky four-sided prisms with oblique ends (rhombic system), without water of crystallisation (*fig. 308, 1*); if it crystallises rapidly it forms delicate white needles. It has no action on litmus, is odourless, and has a weak, bitter, cooling taste, like saltpetre; is readily soluble in water and alcohol, but insoluble in ether. It is an isomer of ammonium cyanate, from which it may be prepared by evaporation, whereby the atoms rearrange themselves (*Wöhler, 1828*). It can be prepared artificially in many other ways.

Decomposition of Urea.—When heated above 120° , it gives off ammonia vapour, while a glassy mass of biuret and cyanic acid is left. When urine undergoes the alkaline fermentation (§ 263), or when urea is treated with strong mineral acids, or boiled with the hydrates of the

alkalies, or superheated with water (240° C.), it takes up two molecules of water and produces ammonium carbonate, thus—



When brought into relation with nitrous acid, it splits up into water, CO_2 , and N. The last two decompositions are made the bases of methods for the quantitative estimation of urea (§ 257).

[**Biuret.**—When urea is heated to 150°–170° C. it melts, gives off ammonia, and the substance which remains is biuret



Biuret with caustic potash and CuSO_4 gives a characteristic rosy solution.]

Quantity.—In normal urine, urea occurs to the extent of 2·5 to 3·2 per cent. An adult man excretes daily from 30 to 40 grms. [500 grains, or a little over 1 oz.]; women less, children relatively more [at 3–6 years, 1 gram; 8–11, .8 gram; and 13–16, .4–.6 gram per kilo. of body-weight]; owing to the relatively greater metabolism in children, the unit weight of body produces more urea than the unit weight of an adult, in the proportion of 1·7 : 1. If the metabolism of the body is in a condition of equilibrium (§ 236), the urea excreted contains almost as much N as is taken in with the nitrogenous constituents of the food (p. 439).

Variations in the Quantity.—The amount of urea increases when the amount of proteids in the food is increased; and also when there is a more rapid breaking up of the nitrogenous tissues of the body itself. As this breaking up is increased by diminution of O, and by loss of blood, so these conditions also increase the urea (§ 41). It is also increased by drinking large draughts of water, by various salts, by frequent urination, and by exposure to compressed air. In diabetic persons, who eat very large quantities of food, it may exceed 110 grms. [over 3 oz.] per day; during hunger it sinks to 6·1 grms. [90 grains] per day. During inanition, the maximum amount is excreted towards mid-day, and the minimum in the morning. The daily amount of urea varies with the quantity of urine; three to four hours after a meal, the formation of urea is at a maximum, when it sinks and reaches its minimum during the night. **Muscular exercise**, as a rule, does not increase it (*v. Voit, Fick and Wislicenus*) although Pflüger states that greatly increased muscular activity increases the urea, and in the same proportion the total N excreted by the urine (§ 295).

Pathological.—In acute febrile inflammations, and in fevers generally (§ 220, 3), the urea increases until the crisis is reached, and afterwards it diminishes. After the fever has passed off, the amount excreted is often under the normal. In some cases of high fever, although the amount of urea formed is increased, it may not be excreted; there is a *retention of the urea*, which, later on, may lead to an increased excretion (*Naunyn*). In chronic diseases, the amount depends largely upon the state of the nutrition, the metabolism, and also upon the degree of fever present. Degenerative changes in the liver, *e.g.*, due to poisoning with phosphorus, may

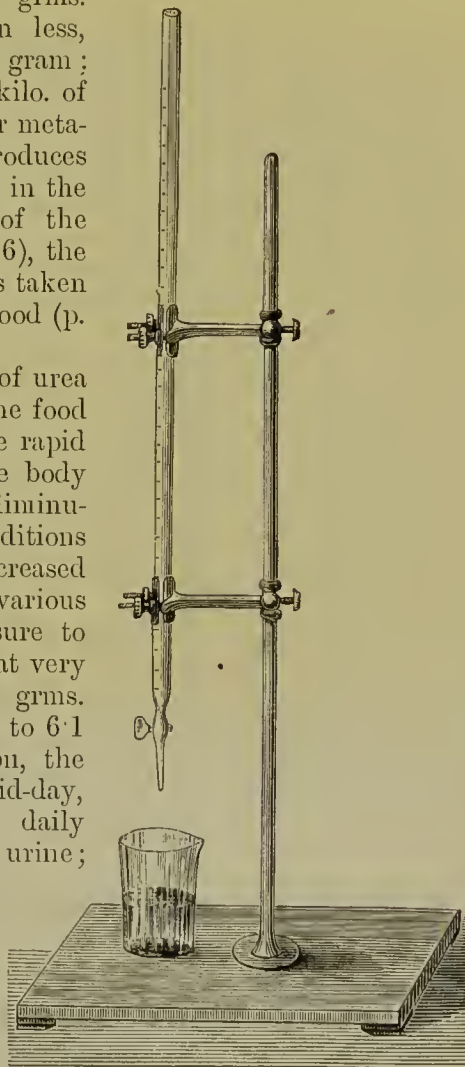


Fig. 307.

Graduated burette.

be accompanied by diminished excretion of urea and increased excretion of ammonia (*Stadelmann*). It is increased in man by morphia, narcotin, narcein, papaverin, codein, thebain (*Erubini*), arsenic (*Gäthgens*), compounds of antimony, and small doses of phosphorus (*Bauer*), which favour the decomposition of proteids, and by substances which increase the bile formation in the liver (*N. Paton*). Quinine, which "spares" the proteids, diminishes it.

Occurrence.—Urea occurs in the blood (1 : 10,000), lymph, chyle, (2 : 1000), liver, lymph-glands, spleen, lungs, brain, eye, bile, saliva, amniotic fluid, and pathologically in sweat, *e.g.*, in cholera, in the vomit and sweat of uræmic patients, and in dropsical fluids.

Formation of Urea.—It is certain that it is the chief end-product of the metabolism of the proteids. Less oxidised products are uric acid, guanin, xanthin, hypoxanthin, alloxan, allantoin, [but it does not follow that these are precursors of urea]. Uric acid administered internally appears in the urine as urea; alloxan and hypoxanthin can be directly changed into urea. The urea excretion is increased by the administration of leucin, glycine, aspartic acid, or ammonia salts (*Schulzen, Nencki*). As yet it has not been definitely determined where urea is formed, but the liver, and, perhaps, the lymph-glands, are organs where it is produced (§ 178).

In birds the liver forms uric acid from ammonia. The liver can be readily excluded from the circulation in birds, and Minkowski found that after this operation the uric acid was diminished and the ammoniacal salts were increased (§ 178).

Antecedents of Urea.—During digestion, part of the proteids is converted into leucin, tyrosin, glycine, and aspartic acid. If the amido-acids, glycine, leucin, or

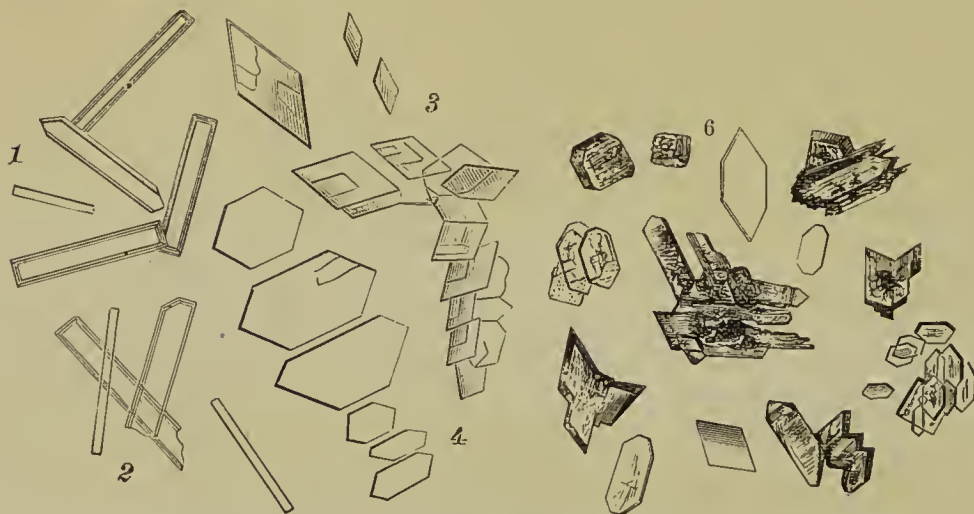


Fig. 308.

1, 2, Prisms of pure urea; 3, rhomboidal plates; 4, hexagonal tablets; 5, 6, irregular scales and plates of urea nitrate.

aspartic acid, or ammoniacal salts be given to an animal, the amount of urea excreted is increased. As the molecule of the amido-acids contains only one atom of N, and the molecule of urea contains two of N, it is probable that urea may be formed *synthetically* from these acids. It is possible that the amido-acids meet with nitrogenous residues in the juices of the body, *e.g.*, carbamic acid or cyanic acid. The union of these may produce urea. According to Salkowski, feeding with these substances causes the breaking up of the proper proteids of the body so as to provide the necessary components. Schmiedeberg is of opinion that urea is formed in the body from ammonium carbonate by the removal of water; and v. Selröder found that when he passed blood containing ammonia carbonate through a "surviving" liver the urea in the blood was greatly increased. Drechsel succeeded in producing urea at ordinary temperatures by the rapid alternating oxidation and reduction of a

watery solution of ammonium carbonate. [We know that the greater part of the urea exists in the blood, and that the renal epithelium removes it from the blood. Although it is surmised that some of the nitrogenous bodies named above, more especially leucin, and perhaps also kreatin, are the precursors of urea, yet we cannot say definitely how or where the transformation takes place. Perhaps this is effected in the liver, and, it may be, also in the spleen (§ 193).]

Preparation of Urea.—Urea may be prepared from dog's urine (especially after a diet of flesh) by evaporating it to a syrupy consistence, extracting it with alcohol, and again evaporating the filtrate to a syrupy consistence. The crystals which separate are washed with water to remove any extractives that may be mixed with them, and dissolved in absolute alcohol. It is then filtered and allowed to crystallise slowly.

Or, human urine may be evaporated to one-sixth of its volume and cooled to 0° , and excess of strong pure nitric acid added, which precipitates urea nitrate mixed with colouring matter. This precipitate is pressed in blotting-paper, then dissolved in boiling water containing animal charcoal, and filtered while hot. When it cools, colourless crystals of urea nitrate separate (fig. 308). These crystals are redissolved in warm water, and barium carbonate added until effervescence ceases; urea and barium carbonate are formed. Evaporate to dryness, extract with absolute alcohol, filter, and allow evaporation to take place, when urea separates.

Compounds of Urea.—Urea combines with acids—nitric, oxalic, phosphoric—bases, and salts (NaCl, nitrate of mercury). The following are the most important combinations:—

1. **Urea nitrate** ($\text{CH}_4\text{N}_2\text{O}$, HNO_3) is easily soluble in water, and not so soluble in water containing nitric acid. It forms characteristic rhombic crystals (fig. 308, 3, 4, 5, 6). Sometimes the formation of these crystals is used to determine microscopically the presence of urea in a fluid. If a fluid is suspected to contain minute traces of urea, it is concentrated and a drop of the fluid is put on a microscopic slide. A thread is placed in the fluid, and the whole is covered with a cover-glass. A drop of concentrated nitric acid is allowed to flow under the cover-glass, and after a time crystals of urea nitrate adhering to the thread may be detected with the microscope.

2. **Urea oxalate** ($\text{CH}_4\text{N}_2\text{O}$)₂, $\text{C}_2\text{H}_2\text{O}_4 + \text{H}_2\text{O}$, is made by mixing a concentrated solution of urea with oxalic acid. The crystals form groups of rhombic tables, often of irregular shape. It is only slightly soluble in cold water, and still less so in alcohol (fig. 309).

3. **Urea phosphate** ($\text{CH}_4\text{N}_2\text{O}$, H_3PO_4), forms large, glancing, rhombic crystals, very easily soluble in water. It is obtained by evaporating the urine of pigs fed on dough.

4. **Sodic chloride + urea** ($\text{CH}_4\text{N}_2\text{O}$, $\text{NaCl} + \text{H}_2\text{O}$) forms rhombic, shining prisms, which are sometimes deposited in evaporated human urine.

5. **Urea + mercuric nitrate** is obtained as a white cheesy precipitate, when mercuric nitrate is added to a solution of urea. Liebig's titration method for urea depends on this reaction (§ 257, II.).

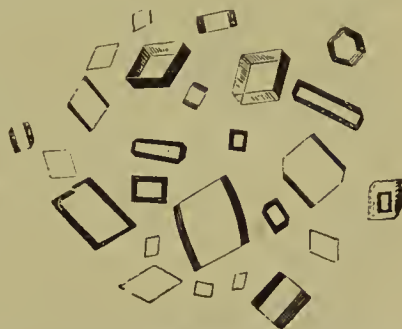


Fig. 309.

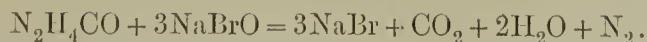
Perfect crystals of oxalate of urea.

257. QUALITATIVE AND QUANTITATIVE ESTIMATION OF UREA.—

I. The qualitative Estimation of Urea.—(1) *It may be isolated as such.* If *albumin* be present, add to the fluid three or four times its volume of alcohol, and, after several hours, filter. Evaporate the filtrate over a water-bath, and dissolve the residue in a few drops of water.

(2) The crystals of **urea nitrate** may be detected microscopically (fig. 308).

II. Quantitative Estimation.—(1) **Sodic hypobromite** decomposes urea into CO_2 , H_2O , and N . On this reaction depends the Knop-Hüfner method of quantitative estimation. The N rises in the form of small bubbles in the mixed fluid, while the CO_2 is absorbed by the caustic soda. [The reaction is the following:—



The nitrogen is collected and estimated in a graduated tube, and the amount of urea calculated from the volume of nitrogen. The uric acid is also decomposed,

but that can be estimated separately and a correction made. We may use the apparatus of Russell and West, or Dupré, or that of Charteris (fig. 310).]

[Ureameter.—Make a solution of hypobromite of soda by mixing 100 grams NaHO in 250 c.c. of water, and adding 25 c.c. of bromine. It is better to be made fresh, as it decomposes by keeping. The graduated tube is placed in a cylindrical vessel, filled with water, and depressed until the zero on the tube coincides with the level of the water. Introduce 15 c.c. of the hypobromite solution into the pyramidal-shaped bottle, while into a short test-tube are placed 5 c.c. of urine. The test-tube with the urine is introduced into the bottle by means of a pair of forceps in such a way that it does not spill. Close the bottle tightly with the caoutchouc stopper, through which passes a glass tube to connect it with the graduated burette. Incline the bottle so as to allow the urine to mix with the hypobromite solution when the gases are given off, and pass into the collecting tube, which is gradually raised until the surfaces of the liquids, outside and in, coincide. Time should be allowed to permit the whole

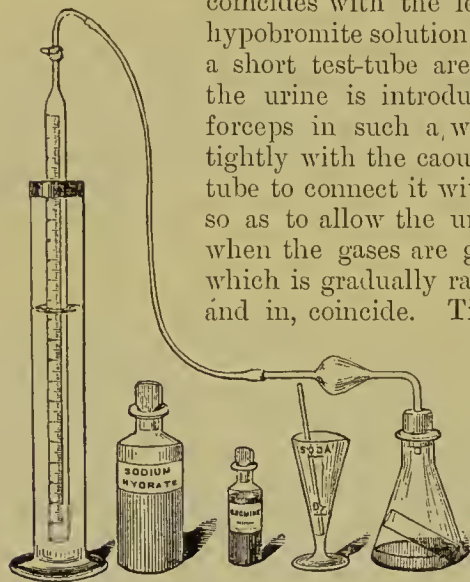


Fig. 310.

Ureameter of Charteris.

e.c., then 30.3 e.c. of $N = 0.1$ gm. of urea at the ordinary temperature and pressure.]

III. Volumetric Method (Liebig).—By means of a graduated pipette (fig. 311), 40 cubic centimetres of the urine are placed in a beaker; add 20 cubic centimetres of barium mixture to precipitate the sulphuric and phosphoric acids. The barium mixture consists of 1 vol. of a cold saturated solution of barium nitrate and 2 vols. of a cold saturated solution of barium hydrate. Filter through a dry filter, and take 15 cubic centimetres of the filtrate, which correspond to 10 e.c. of urine, and place in a beaker. Allow a titrated standard solution of mercuric nitrate to drop from a burette into the urine until a precipitate no longer occurs. The mercuric nitrate is made of such a strength that 1 cubic centimetre of it will combine with 10 milligramms of urea. Test a drop of the mixture from time to time with a solution of sodic carbonate, which is called the indicator, and placed in a watch-glass or piece of glass blackened on its under surface. Whenever the slightest excess of mercuric nitrate is added, the mixture strikes a yellow colour with the soda. The standard solution must be added drop by drop until this result is obtained. Read off the number of cubic centimetres of the standard solution used; as each centimetre corresponds to 10 milligramms of urea, multiply by ten, and the amount of urea in 10 cubic centimetres of urine is obtained.

This method does not give quite accurate results even in normal urine. To urine containing much phosphates is added an equal volume of the barium mixture. Very acid urines may require several volumes to be added. Urine containing albumin or blood must be boiled, after the addition of a few drops of acetic acid, to remove the albumin. The sodic chloride in the urine also interferes with the accuracy of the process, as, on adding mercuric nitrate to urine, mercuric chloride and sodic nitrate are formed, so that the urea does not combine until the sodic chloride is decomposed. When the urine contains, as is usually the case, 1 to $1\frac{1}{2}$ per cent. NaCl, deduct 2 c.c. from the number of c.c. of the S.S. added to 10 c.c. of urine.

Estimation of the total N in Urine (Kjeldahl's Method).—Pflüger and Bohland recommend the following modification of the method of Kjeldahl. Five c.c. of a urine of medium concentration are allowed to flow from a burette into Erlenmeyer's flask, capable of containing about 300 c.c., and to it are added 20 c.c. of concentrated sulphuric acid. The whole is boiled until all the water and gases are driven off. The fluid at first becomes black from the action of the sulphuric acid, but when it has become of brownish tone lessen the heat of the Bunsen

burner. About half an hour suffices to heat it, when the fluid at last becomes bright yellow. Allow it to cool, dilute it with water to 200 c.c., and place the whole in a flask, add 80 c.c. of caustic soda (S.G. 1·3), cork the flask as quickly as possible, and distil its contents. The distillate must pass over into sulphuric acid, which must be titrated beforehand. The quantity of sulphuric acid not combined with ammonia must be estimated by titration with caustic soda.

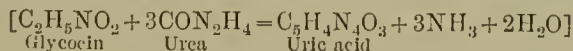
The N in the Urine may be estimated approximately thus. To 10 c.c. of the urine add from a burette Liebig's mercuric nitrate solution, and test the mixture on a black glass plate with dry sodic bicarbonate until a yellow speck remains. Multiply the number of c.c. of the burette fluid used by 0·04 (*Pflüger and Bohland*).

258. URIC ACID = $C_5H_4N_4O_3$ is the nitrogenous substance which, next to urea, carries off most of the N from the body; in twenty-four hours 0·5 gm. (7 to 10 grains); during hunger, 0·24 gm. (4 grains); after a strongly animal diet, 2·11 gm. (30 to 35 grains) are excreted; [on a purely vegetable diet it amounts to 0·2 to 0·7 gram.] The proportion of urea to uric acid is 45 : 1.

If a mammal be fed with uric acid, part of it becomes more highly oxidised into urea, while the oxalic acid in the urine is also increased (§ 260); in fowls, feeding with leucin, glycine, or aspartic acid (*v. Knieriem*), or ammonium carbonate (*Schroeder*), increases the amount of uric acid. When urea is administered to fowls, it is *reduced* chiefly to uric acid. The fresh splenic pulp containing so many decomposition products of leucocytes (nuclein, xanthin-bodies, p. 169) (§ 169) when treated with warm blood yields it (*Horbaczewski*). It is the chief nitrogenous product in the urine of birds, reptiles, and insects. It is sometimes, but not always, absent from herbivorous urine.

Properties.—It is dibasic, colourless, and crystallises in various forms (figs. 312 and 313), belonging to the **rhombic system** (1). When the angles are rounded, the *whetstone* form (2) is produced, and if the long surfaces be flattened, six-sided tables occur. Not unfrequently diabetic urine deposits spontaneously large, yellow, transparent rosettes (6, 8). If 20 c.c. of HCl, or acetic acid, be added to 1 litre of urine, crystals (9) are deposited, like cayenne pepper, on the surface and sides of the glass, *after several hours*. [The HCl decomposes the urates, and liberates the acid, which does not crystallise at once, owing to the presence of the phosphates in the urine. Crystals of uric acid are usually yellowish in colour from the pigment of the urine (fig. 312), and they are soluble in caustic potash.]

Solubility.—It is tasteless and odourless; reddens litmus; is soluble in 15,000 parts of cold and in 1900 of boiling water, and insoluble in alcohol and ether. *Horbaczewski* prepared it synthetically by melting together glycine, or, as it is also called, glycocin, and urea.



It is freely soluble in alkaline carbonates, borates, phosphates, lactates, and acetates, these salts at the same time removing a part of the base; thus there are formed acid urates and acid salts from the neutral salts. It is soluble in concentrated sulphuric acid, from which it may be precipitated by the addition of water. [The phosphates play an important part in keeping it in solution in the urine.]

Decomposition.—During dry distillation it decomposes into urea, cyanuric acid, hydrocyanic acid, and ammonium carbonate. Superoxide of lead converts it into urea, allantoin, oxalic acid, and CO₂; while ozone forms the same substances, with the addition of alloxan. When it is reduced by H *in statu nascenti*, as by sodium amalgam, it forms xanthin and sarkin. It is a less oxidised metabolic product than urea, but it is by no means proved that uric acid is a precursor of urea.

Occurrence.—Uric acid occurs dissolved in the urine in the form of **acid urates of soda and potash**. These salts occur also in urinary calculi, gravel, and in gouty



Fig. 311.
Graduated
Pipette.

deposits. Ammonium urate occurs in very small quantity in a deposit of "urates," but is formed in considerable amount when urine becomes ammoniacal from decomposition (fig. 317). *Free uric acid* occurs in normal urine only in the very smallest amount. It is sometimes deposited *after a time* (fig. 316). It frequently forms urinary calculi and gravel.

The urine of newly-born children contains much uric acid. Uric acid and its salts are increased after severe muscular exertion, accompanied by perspiration, in catarrhal and rheumatic fevers, and such conditions as are accompanied by disturbance of the respiration; in leukæmia and tumours of the spleen cirrhotic liver, and generally in cases of catarrh of the



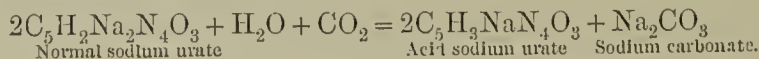
Fig. 312.

Forms of uric acid. 1. Rhombic plates; 2, whetstone forms; 3, quadrate forms; 4, 5, prolonged into points; 6, 8, rosettes; 7, pointed bundles; 9, barrel forms precipitated by adding hydrochloric acid to urine.

stomach and intestinal tract, following the excessive use of alcohol. [It is certainly increased in leukæmia, as much as 4 grams have been eliminated in 24 hours. It is also increased during ague and fevers, and perhaps this has some relation to the congestion of the spleen which accompanies these conditions.] It is diminished after copious draughts of water, after large doses of quinine, caffeine, potassic iodide, common salt, sodic and lithic carbonates, sodic sulphate, inhalation of O, slight muscular exertion. In gout, the amount excreted in the urine is small. In chronic tumours of the spleen, anæmia, and chlorosis, when the respiration is not at the same time embarrassed, it is also diminished.

[The quantity of uric acid excreted is greatest during the "alkaline tide." By the use of acids the uric acid is relatively diminished. Suppose the normal ratio of uric acid to urea to be 1 : 35, then after the use of acids (4 grams of citric acid three times daily), the proportion will be about 1 : 41. If alkalies be taken, (3 grams citrate of potash three times daily) the reverse is the case, the ratio becomes about 1 : 28 (*Huig*).]

Urates.—Uric acid forms salts—chiefly *acid* urates—with several bases, which dissolve with difficulty in cold water, but are easily soluble in warm water. Neutral urates are changed by CO₂ into acid salts. [The urates are insoluble substances and are readily precipitated, but this occurs more readily during the acid formation of urine, because the acid urate of sodium is then formed, and it is more insoluble than the normal urate—



Hydrochloric and acetic acids break up the compounds, and crystals of uric acid separate. [According to W. Roberts uric acid is perhaps a vestigial remnant in

mammalian descent. Besides the acid and normal urates Roberts describes what he calls quadrurates, and he regards them as the exclusive combination in which uric acid exists in solution in normal urine. The appearance of a deposit of urates in urine when it cools does not necessarily mean that there is an increased formation of urates, for urates may be deposited in concentrated urine when it cools.]

[One of the atoms of H is easily replaced by metals. If uric acid be dissolved in sodic carbonate we obtain $C_5H_3NaN_4O_3$ which is an **acid urate**. If, however, it be dissolved in an alkali, *e.g.*, caustic soda, we get $C_5H_2Na_2N_4O_3$ whereby a second atom of H is replaced by an alkaline metal, producing "**neutral or normal urate**." It is not known if the latter action occurs in the body.]

(1) **Acid sodic urate** usually appears as a brick-red deposit in urine; more rarely grey or white (lateritious deposit), tinged with uroerythrin, in catarrhal conditions of the digestive organs, and in rheumatic and febrile affections. **Microscopically**, it is completely amorphous, consisting of granules, sometimes disposed in groups (fig. 316, *b*)—sometimes the granules have spines on them. The corresponding potash salt occurs not unfrequently under the same conditions, and presents the same characters.

(2) **Acid ammonium urate** (fig. 317, *a*) always occurs as a sediment in ammoniacal urine, either with (1), or mixed with free uric acid, accompanied by triple phosphate. Microscopically, it is the same as (1). (1) and (2) are distinguished by the sediment dissolving when the urine is heated. If a drop of hydrochloric acid be added to a microscopic preparation of the sediment, crystals of uric acid separate.

(3) **Acid calcic urate** occurs sometimes in calculi, and is a white, amorphous powder slightly soluble in water. When heated on platinum it leaves an ash of calcium carbonate. Magnesium urate rarely occurs in urinary calculi.

[A deposit of urates is of common occurrence in urine, *e.g.*, after excessive muscular exercise, deranged digestion, &c. They exist in urine chiefly as normal sodium urate, but they are deposited chiefly as acid urates when the urine cools. The deposit is often pink coloured and is chiefly amorphous, but it may contain a few crystals. It redissolves when the urine is heated. The following table gives the chief facts relative to the urates (*Ralfe*):—

Urates.	Formulae.	Solubility in water.	Deposited as
Acid ammonium urate, .	$C_5H_3N_4O_3.(NH_4)$	1 in 1600	Amorphous or spiked globular masses.
Normal sodium " "	$C_5H_2N_4O_3.Na_2$	1 in 77	Nodular masses.
Acid " "	$C_5H_3N_4O_3.Na$	1 in 1200	Amorphous, rarely crystalline.
Normal potassium " "	$C_5H_2N_4O_3.K_2$	1 in 44	Amorphous, or in fine needles.
Acid " "	$C_5H_3N_4O_3.K$	1 in 800	...
Normal calcium " "	$C_5H_2N_4O_3.Ca$	1 in 1500	Fine granules.
Acid " "	$(C_5H_3N_4O_3)_2.Ca$	1 in 600	Amorphous, or in fine needles.
Acid lithium " "	$C_5H_3N_4O_3.Li$	1 in 60	" " "

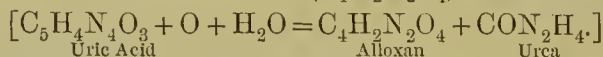
The greater solubility of lithium and potassium urates has led to the administration of potash or lithia water in cases of uric acid diathesis.]

[**Formation of Uric Acid.**—It exists in the blood, and does not seem to be formed in the kidneys. In gout, when there is a diminished excretion of uric acid it accumulates in the blood and tissues. After extirpation of the kidneys in birds and snakes, it accumulates in the blood and organs. The seat of its formation in mammals has not been ascertained experimentally. In **birds**, however, it seems to be formed in the **liver**. Birds have a vascular system in their kidneys similar to the portal vein. A vena advehens carries the blood from the caudal and iliac veins and veins coming from the pelvic viscera to the kidneys, and the vena advehens communicates with the portal vein by means of Jacobson's vein. Minkowski tied the portal vein in geese, thus excluding the liver, but the blood from the abdominal organs still passed through the kidneys to the inferior vena cava. The animals lived from 6–20 hours. He found that the total nitrogen eliminated in the urine is not greatly diminished (reduced about one-half or less),

but the proportion of uric acid to the total nitrogen was greatly diminished. Normally, in geese 60–70 per cent. of the total nitrogen in the urine is eliminated as uric acid, but after exclusion of the liver it amounts only to 3–6 per cent., while the ammonia is enormously increased. The normal 9–18 per cent. of ammonia is increased to 50–60 per cent. It would seem as if ammonia is a normal antecedent of uric acid, and that the synthesis perhaps takes place in the liver. Another noteworthy fact observed was the simultaneous great increase of lactic acid in the urine (p. 492).]

259. ESTIMATION OF URIC ACID.—I. Qualitative.—1. **Microscopic Characters.**—The appearances presented by uric acid and its salts under the microscope are shown in fig. 313. It is deposited from urine after several hours, on adding acetic or hydrochloric acid.

2. **Murexide Test.**—Gently heat a urate or uric acid in a porcelain vessel along with nitric acid. Decomposition takes place and the colour changes to yellow. N and CO₂ are given off; urea and alloxan (C₄H₂N₂O₄) remain.



Evaporate slowly and allow the yellowish-red stain to cool; on adding a drop of dilute ammonia a *purplish-red* colour of murexide (which contains furfurate of ammonia, alloxantin-amid) is obtained, it becomes blue on the addition of caustic potash. If potash or soda be added instead of ammonia, a violet colour is obtained, which disappears on heating.

3. **Schiff's Test.**—Dissolve uric acid or a urate in a solution of an alkaline carbonate, and drop it upon blotting-paper saturated with a solution of *silver nitrate*; reduction of the silver takes place at once, and a black spot is formed.

4. On boiling a solution of uric acid or a urate in an alkali, with Fehling's solution (§ 149, 2), at first white urate of the suboxide of copper is deposited, while later, red copper suboxide is formed.

II. Quantitative Estimation.—Add 5 cubic centimetres of concentrated HCl to 100 c.c. of urine, and allow it to stand for forty-eight hours in the dark, when the uric acid is precipitated like fine cayenne pepper crystals. All the uric acid is not precipitated by the HCl, even after standing for a time. [E. A. Cook uses sulphate of zinc to precipitate the uric acid as urate of zinc. Caustic soda is added to precipitate the phosphates, and then to the clear fluid zinc sulphate solution, which precipitates urate of zinc as a white gelatinous deposit.]

Fokker-Salkowski Method.—Make 200 c.c. of urine strongly alkaline with sodic carbonate, and after an hour add 200 c.c. of a concentrated solution of ammonium chloride, whereby acid urate of ammonium is precipitated. After forty-eight hours filter through a small weighed filter, and wash it several times. Fill the filter with dilute HCl and collect the filtrate. Do this until all the acid urate is dissolved. From the total filtrate after a time all the uric acid separates. It is collected on the same filter, washed with water and alcohol until the acid reaction disappears, dried at 100° C, and weighed. To the weight in excess of the filter add 0.030 gm.

[Haycraft's method depends on the fact, that uric acid forms a compound with silver—urate of silver—which is very insoluble in water. The solutions required are:—1. Centinormal ammoniac sulphocyanate, made by dissolving 8 grms. of crystals in 1 litre of water, and adjust to decinormal silver solution. Dilute with 9 vols. of water, 1 c.c.=0.00168 uric acid. 2. Saturated solution of iron-alum (the indicator). 3. Pure HNO₃ (20 to 30 per cent.). 4. Strong ammonia. Ammoniacal silver solution made by dissolving 5 grms. AgNO₃ in 100 c.c. water, and add NH₄HO until the solution becomes clear. **Process.**—Place 25 c.c. of urine in a beaker, and add 1 gm. sodie bicarbonate; then add 2 to 3 c.c. of ammonia to precipitate ammonio-magnesian phosphate. Add 1 to 2 c.c. of ammoniacal silver solution, which precipitates silver urate in a white gelatinous form. The precipitate is then thoroughly washed on an asbestos filter, and then dissolved from this by nitric acid, after which the silver is estimated (Volhard's method). In doing so, add a few drops of the indicator, and drop in the centinormal solution of ammoniac sulphocyanate. A white precipitate with a transient reddish coloration will be formed; as soon as the red colour is permanent the process is at an end. The uric acid present is ascertained by multiplying the number of cubic centimetres of the sulphocyanate used by 0.00168.

260. KREATININ AND OTHER SUBSTANCES.—Kreatinin C₄H₇N₃O, is

derived from the kreatin of muscle by the removal of a molecule of water, and partly from flesh food. The quantity excreted daily is 0.6 to 1.3 gram (8 to 18 grains).

[Source.—It is generally considered that it is formed from the kreatin of muscle. If kreatin be given to animals by the mouth it reappears in the urine as kreatinin, but if it be injected into the blood stream it reappears as kreatin, so that the kidneys cannot effect the change. Perhaps the change is effected in the muscles.]

It is diminished in progressive muscular atrophy, tetanus, anæmia, marasmus, chlorosis, consumption, paralysis; and is increased in typhus, inflammation of the lung; it is absent from the urine of sucklings.

Properties.—Kreatinin is alkaline, easily soluble in water and hot alcohol. It forms colourless oblique rhombic columns; unites with acids and salts, silver nitrate, mercuric chloride, and especially with *zinc chloride*.

Tests.—Kreatinin-zinc chloride (fig. 313) is used to detect its presence. **Weyl's Test.**—Add to urine a few drops of a slightly brownish solution of nitro-prusside of soda, and then weak caustic soda solution, producing a Burgundy-red colour, which soon disappears. When heated with glacial acetic acid, the colour changes to green, which after a time changes to blue (*Salkowski*). Aceton gives a similar reaction, but in this case the red colour is darker, and more of a purple shade. Aceton can be expelled by boiling the urine; so that it is better to boil the urine beforehand, if aceton be suspected. [The blue colour—Berlin blue—is due to the formation of an iron-salt, ferrocyanide of sodium, from the decomposition of the nitro-prusside. The reaction also succeeds with formic acid—instead of glacial acetic acid—if some time be allowed to elapse after Weyl's reaction.]

Xanthin— $C_5H_4N_4O_2$ occurs only to the amount of 1 gram in 300 kilos. of urine. It is a substance intermediate between sarkin and uric acid. Guanin and hypoxanthin may be changed into xanthin; in contact with water and ferments it passes into uric acid. When evaporated with nitric acid, it gives a yellow stain, which becomes yellowish-red on adding potash, and violet-red on applying more heat. It is an amorphous, yellowish-white powder, fairly soluble in boiling water. It has also been found in traces in muscles, brain, liver, spleen, pancreas, and thymus. The crystalline body **paraxanthin** (dimethylxanthin) and the amorphous **heteroxanthin** (methylxanthin) occur in traces in the urine (*Salomon*).

Sarkin or Hypoxanthin, $C_5H_4N_4O$.—As yet this substance has been found only in the urine of leukaemic patients (*Jakubasch*), and it has been prepared in the form of needles or flattened scales from muscle, spleen, thymus, brain, bone, liver, and kidney. In normal urine a body nearly related to, and possibly identical with, hypoxanthin occurs (*E. Salkowski*). Hypoxanthin closely resembles xanthin, and can be changed into it by oxidation. Nascent hydrogen, on the other hand, reduces uric acid to xanthin and hypoxanthin. When evaporated with nitric acid it gives a light yellow stain, which becomes deeper, but not reddish-yellow, on adding caustic soda. It is more easily soluble in water than xanthin, and by this means the two substances can be separated from each other. Guanin is insoluble in water.

[Notice the close relation of the three bodies—uric acid, xanthin, and hypoxanthin. The difference is in the proportion of oxygen:—

Uric acid, ...	$C_5H_4N_4O_3$
Xanthin, ...	$C_5H_4N_4O_2$
Hypoxanthin, ...	$C_5H_4N_4O$

Closely related to these, and belonging to the xanthin group, but which do not occur in urine, are *guanin*, ($C_5H_5N_5O$) and *adenin* ($C_5H_5N_5$), the latter a polymer of hydrocyanic acid. Perhaps all these four bodies belong to the antecedents of urica or uric acid (*Bunge*).]

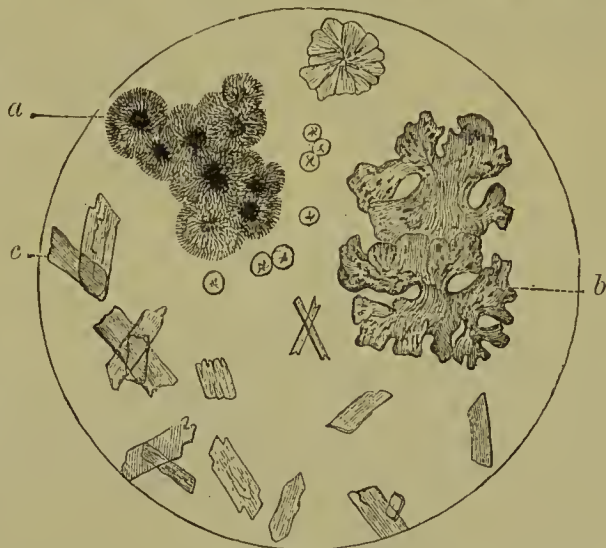


Fig. 313.

Kreatinin-zinc chloride. *a*, balls with radiating marks; *b*, crystallised from water; *c*, from alcohol.

Oxaluric acid ($C_3H_4N_2O_4$) is an oxidation product of uric acid, and occurs in *very small quantity* combined with ammonia in urine. Physiologically, it is interesting on account of its relation to uric acid. It is a white powder slightly soluble in water. Ammonium oxalurate can be prepared from uric acid.

Oxalic Acid ($C_2H_2O_4$) occurs, but not constantly, to the amount of 20 milligrams daily, [but never as free oxalic acid]. It is united with calcium and held in solution by the acid phosphate of soda. Sometimes it forms a deposit of **oxalate of lime**, which is known by the "envelope" shape of the crystals (fig. 314); insoluble in acetic acid, and forming transparent octahedra. More rarely it assumes a biscuit or sand-glass form. The genetic relation of oxalic acid to uric acid is shown by the fact, that dogs fed with uric acid excrete much oxalate of lime. Oxalic acid may also be produced by the oxidation of products derived from the fatty acid series (p. 474).

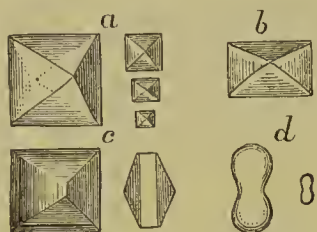


Fig. 314.

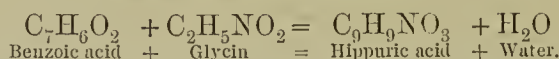
Oxalate of lime. *a*, *b*, octahedra; *c*, compound forms; *d*, dumb-bells.

Oxaluria.—The eating of substances containing oxalate of lime (rhubarb) increases the excretion. Increased excretion is called oxaluria; it is regarded as a sign of retarded metabolism (*Beneke*), and it may give rise to the formation of a calculus. In oxaluria the uric acid is also often increased in amount. Perhaps, in the first instance, there is an increased formation of uric acid, from which oxalic acid, urea, and CO_2 may be formed. The amount of oxalic acid is increased after the use of wine and sodic bicarbonate.

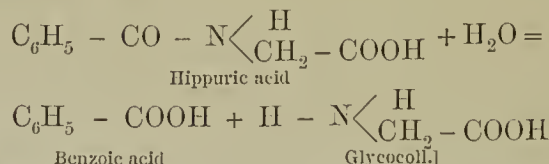
Hippuric Acid = $C_9H_9NO_3$ (Benzoylamidoacetic acid, p. 477) occurs in large amount in the urine of herbivora, and in them is the chief end-product of the metabolism of certain nitrogenous substances; in human urine the daily **quantity** is small, 0.3 to 3.8 grms. (5 to 50 grains). It is an odourless monobasic acid with a bitter taste, crystallising in colourless four-sided prisms (fig. 315). [It exists in urine as hippurates of the alkalies.] Readily soluble in alcohol, and soluble in 600 parts of water. Its presence in urine is a matter of diet.

[Crystals of hippuric acid when heated in a test-tube are decomposed, and a sublimate of benzoic acid and ammonie benzoate condenses on the upper cool part of the tube, while there is an odour of new hay, and oily drops remain in the tube.]

It is a conjugated acid, and is formed in the body from benzoic acid, or some nearly related chemical body, such as the cuticular substance of plants, or from oil of bitter almonds, cinnamic or quinic acid, which easily pass by reduction (quinic acid) or by oxidation (cinnamic acid) into benzoic acid. It may be formed by the union with hydration of **benzoic acid with glycine**:—



[If hippuric acid be boiled with alkalies or strong mineral acid, it splits up with hydration into benzoic acid and glycocholic or glycine.



[Formation of Hippuric Acid.]—When **benzoic acid** is introduced into the alimentary canal of an animal (rabbit or dog), it appears in the urine as hippuric acid, so that somewhere in the body benzoic acid meets with and combines with glycine. Nitro-benzoic acid appears as nitro-hippuric acid. As the benzoic acid passes through the body, it becomes conjugated with glycine or glycocholic, chiefly in the **kidneys**. The hippuric acid in the urine of herbivora is chiefly derived from some substance with a benzoic acid residue—the aromatic combinations—present

in the cuticular coverings of the food. That hippuric acid, in part at least, is formed in the kidneys, *i.e.*, by the cells of the renal tubules, is shown by the following considerations:—If arterialised blood, containing benzoic acid and glycin, or even benzoic acid alone, be passed through the blood-vessels of a fresh, living, excised kidney, a so-called “surviving kidney,” hippuric acid is found in the blood after it is perfused. Even after forty-eight hours, if the kidney be kept cool, the synthesis takes place. The kidney in this case also must not be dead, but a “surviving” one. If the kidney be kept too long, the conjugation does not take place. If the fresh surviving kidney be chopped up, and kept at the temperature of the body with benzoic acid and glycoll, hippuric acid is formed. Oxygen seems to be necessary for the process, for, if blood or serum containing carbonic oxide be used, there is no formation of hippuric acid.]

[If the liver be excised in frogs, and benzoic acid, or better, benzoic acid and glycoll, be injected into the dorsal lymph-sac, hippuric acid is found in the tissues and secretions. Thus the liver is not the locality, or exclusive locality, in the frog, where the synthesis occurs. But in the frog, it may be formed after extirpation of the kidneys. It is only in the dog that its exclusive formation in the kidney has been proved (*Bunge and Schmiedeberg*).]

[There is one difficulty about the matter, *viz.*, that glycin, as such, has not been found in the tissues. It is probable, however, that it is formed in various metabolic processes, and is as rapidly combined with some other body. It may be formed in this way in the kidney, and immediately combine with benzoic acid to form hippuric acid.]

According to this view, it is derived chiefly from the food of herbivorous animals, and hence it is absent from the urine of sucking calves, as well as after feeding with grain devoid of husk. But it is also formed in the body from the proteids. In the dog, the formation of hippuric acid occurs in the kidney (*Schmiedeberg and Bunge*), and in the frog also outside the kidney. Kühne and Hallwachs thought it was formed in the liver, and Jaarsveld and Stockvis in the kidney, liver, and intestine. The observation of Salomon that, after excision of the kidneys in rabbits, and injection of benzoic acid into the blood, hippuric acid was found in the muscles, blood, and liver, goes to show that it must be formed in other organs beside the kidneys. The power of changing benzoic acid introduced into the human body into hippuric acid may even be abolished in disease of the kidney. Under certain circumstances it seems that hippuric acid, already formed, may be again decomposed in the tissues.

It is greatly increased after eating pears, plums, and cranberries; in icterus, some liver affections, and in diabetes.

Preparation.—Add milk of lime to the *fresh* urine of horses or cows to form calcic hippurate. Filter, evaporate the filtrate to a small bulk, and precipitate the hippuric acid with excess of hydrochloric acid. To purify the hippuric acid, crystallise it several times from a hot watery solution.

Cynuric Acid $C_{20}H_{14}N_2O_6 + H_2O$ occurs in the urine of dogs (*J. v. Liebig*).

Allantoin, $C_4H_4N_4O_3$, which occurs in the amniotic fluid of the cow, is found in minute traces in normal urine after flesh food, and is more abundant during the first weeks of life and during pregnancy. [It to a large extent replaces urea in the urine of the fœtus.]

After large doses of tannic acid the amount is increased (*Schottin*), while, in dogs, feeding with uric acid also increases it (*Sulkowski*).

Properties.—It forms shining, prismatic crystals; from the urine of sucking calves it crystallises in transparent prisms. It is decomposed by ferments into urea, ammonium oxalate, and carbonate, and another as yet unknown body. **Preparation**—(a) the urine is precipitated

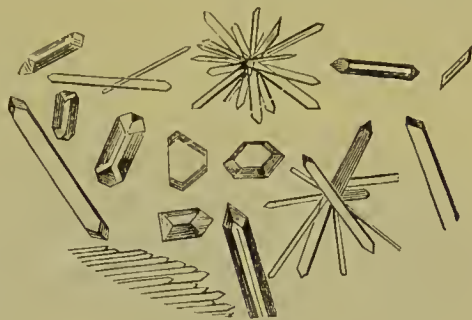


Fig. 315.

Hippuric Acid.

with basic lead acetate, the lead in the filtrate is removed by sulphuretted hydrogen, and the filtrate itself is then evaporated to a syrup, from which the crystals separate, after standing for several days. They are then washed with water, and recrystallised from the water (*Salkowski*).

261. COLOURING-MATTERS OF THE URINE.—1. **Urobilin** is most abundant in the highly-coloured urine of fevers, but it also occurs in normal urine (*Jaffé*). It is identical with the hydrobilirubin of Maly (§ 177, 3, *g*). It is a derivative of hæmatin, which also yields the *bile-pigments* (§ 177). It gives a *red*, or *reddish-yellow*, colour to urine, which becomes yellow on the addition of ammonia. [What is called **normal bilirubin** seems to be the principal colouring-matter in urine.]

[MacMunn, chiefly from spectroscopic observations, finds that two entirely different substances have been included under the name of “**urobilin**,” viz., that of normal and that of pathological urine, and that hydrobilirubin is not identical with either. The pathological urobilin seems to be closely connected with stercobilin (§ 185).]

Preparation.—Prepare a chloroform extract of urine containing urobilin—add iodine to the extract, and remove the iodine by shaking the mixture with dilute caustic potash, which forms potassic iodide. This potash solution becomes yellow or brownish-yellow, and exhibits beautiful green *fluorescence* (*Gerhardt*).

Urobilin may be extracted from many urines by ether (*Salkowski*). When subjected to the action of reducing agents, *e.g.*, sodium amalgam, a colourless product is obtained, which on exposure to the air absorbs O, and becomes retransformed into urobilin. This colourless body is identical with the chromogen which Jaffé found in urine.

If urine is treated with soda or potash, the characteristic absorption-band lying between *b* and *F*. passes nearer to *b*, becomes darker and more sharply defined. According to Hoppe-Seyler, urobilin is formed in urine after it is voided, from another urobilin-forming body (*Jaffé*'s chromogen) absorbing oxygen. If urine containing urobilin be made alkaline with ammonia, and zinc chloride be added, it exhibits marked *fluorescence*; it has a *green* shimmer by reflected light. When urobilin is *isolated*, it fluoresces without the addition of zinc chloride. In cases of jaundice (§ 180), where Gmelin's test sometimes fails to reveal the presence of bile-pigments, urobilin occurs. This “**urobilin-icterus**” (*Gerhardt*) occurs chiefly after the absorption of large extravasations of blood. According to Cazenave, the urobilin is increased in all diseases where there is increased disintegration of coloured blood-corpuscles.

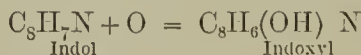
2. **Urochrome** was regarded (*Thudichum*) as the chief colouring-matter of urine. It may be isolated in the form of yellow scales, soluble in water, and in dilute acids and alkalies. [It is possibly impure urobilin.] The watery solution oxidises, and when exposed to air becomes red owing to the formation of **uroerythrin**. When acted on by acids, new decomposition-products are formed, *e.g.*, **uromelanin**. Uroerythrin gives the red colour to deposits of urates (§ 258).

3. A brown pigment containing iron is carried down with uric acid, which is precipitated on the addition of hydrochloric acid (§ 258). By repeatedly adding sodic urate to the urine, and precipitating the uric acid by hydrochloric acid, a considerable amount may be obtained (*Kunkel*).

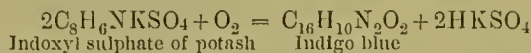
4. Urine boiled with HCl yields a garnet-red crystalline pigment, **urorubin**, to ether.

In cases of melanotic tumours, there has been occasionally observed urine, which becomes dark, owing to melanin (§ 250, 4), or to a colouring-matter containing iron (*Kunkel*).

262. INDIGO, PHENOL, KRESOL, PYROKATECHIN, AND SKATOL-FORMING SUBSTANCES.—1. **Indican**. [$C_8H_7NSO_4$], or indigo-forming substance (*Schunck*), is derived from indol, C_8H_7N , the basis of indigo, which is formed in the intestine by the pancreatic digestion of proteids (§ 170, II.), but it also arises as a putrefactive product (§ 184, III.). Indol, when united with the radical of sulphuric acid, HSO_3 , and combined with potassium, forms the so-called **indigogen** or **indican** of urine (*Brieger, Baumann*). This substance ($C_8H_6NSO_4K$ = potassium indoxyl-sulphate) forms white glazing tablets and plates; readily soluble in water and less so in alcohol. By oxidation it forms indigo-blue; $2 \text{ indican} + O_2 = C_{16}H_{10}N_2O_2$ (indigo-blue) + $2HKSO_4$ (acid potassic sulphate). It is more abundant in the urine in the tropics, and it is absent from the urine of the newly-born (*Senator*). [The indigo in the animal body is derived from indol, the basis of the indigo group. Indol is formed in the intestine by the bacterial putrefaction of proteids, and when absorbed it is oxidised into indoxyl—



Tests.—(1) Add to 40 drops of urine, 3 to 4 c.c. of strong fuming hydrochloric acid, and 2 to 3 drops of nitric acid. Boil, a *violet-red* colour (with the deposition of true *crystalline indigo-blue* (rhombic) and indigo-red attests its presence. Putrefaction causes a similar decomposition in indican; hence, we not unfrequently observe a bluish-red pellicle of microscopic crystals of indigo-blue, or even a precipitate of the same. (2) Mix in a beaker equal quantities of urine and hydrochloric acid, and add two drops of solution of chloride of lime; the mixture at first becomes clear, then blue (*Jaffé*). Add chloroform, and shake the mixture vigorously for some time; the chloroform dissolves the blue colouring-matter, which is obtained as a deposit, when the chloroform evaporates (*Senator, Salkowski*) [What happens in this case is that the indigo exists in urine as a colourless combination—indoxyl-sulphate of potash, the conjugated sulphuric acid is split up, and the indoxyl is oxidised into indigo—



(3) Heat to 70° one part of urine with two parts of nitric acid, and shake up with chloroform; the chloroform dissolves the indigo which is formed, assumes a violet colour, and gives an absorption band between C and D, slightly nearer D (*Hoppe-Seyler*).

Quantity.—Jaffé found in 1500 c.c. of normal human urine, 4·5 to 19·5 milligrams of indigo; horse's urine contains 23 times as much. The subcutaneous injection of indol increases the indican in the urine (*Jaffé*). E. Ludwig obtained indican by heating hæmatin or urobilin with a caustic alkali and zinc dust. It has also been found in the sweat (§ 286) (*Bizio*).

Pathological.—The indican in the urine is increased when much indol is formed in the intestine (§ 170, II.), e.g., in typhus, lead colic, trichinosis, catarrh and hæmorrhage, of the stomach, cholera, carcinoma of the liver and stomach; obstruction of the bowels or ileus, peritonitis, and diseases of the small intestine. [It is a fact of some practical importance that a large quantity of the indoxyl compound, indican, is found in the urine in intestinal obstruction. It is increased after ligature of the small, but not the large, intestine in dogs. This is due to the putrefaction of the albumin in the intestine yielding indol. In man it is increased in obstruction of the small, but not of the large, gut.]

2. Phenol, $\text{C}_6\text{H}_6\text{O}$ (carbolic acid, § 252, IV.), was discovered by Städeler in human urine (more abundant in horse's urine). It does not occur as carbolic acid, but in combination with a substance from which it is separated by distillation with dilute mineral acids. The "phenol-forming substance" is, according to Baumann, "**phenolsulphuric acid**" ($\text{C}_6\text{H}_5\text{O}, \text{SO}_3\text{H}$), which in urine is united with potash [*i.e.*, as **phenol-sulphate of potassium**, $\text{C}_6\text{H}_5\text{O} \cdot \text{SO}_3\text{K}$.]

Phenol is derived from the decomposition of proteids by pancreatic digestion (§ 170, II.), and also from putrefaction (§ 184, III.), the mother-substance being tyrosin. Hence, the formation of phenolsulphuric acid is analogous to the formation of indican.

If in the employment of carbolic acid it be absorbed, the phenolsulphuric acid becomes greatly increased in amount, so that sulphuric acid must be united with it; hence, alkaline sulphates are decomposed in the body, so that the latter may be absent from the urine (*Baumann*). Living muscle or liver, when digested in a stream of air for several hours with blood to which phenol and sodic sulphate are added, yields phenolsulphuric acid; while, under the same circumstances, pyrocatechin forms ethersulphuric acid.

Carbouluria.—When carbolic acid is used externally or internally, and it is absorbed, it causes a *deep dark-coloured* urine due to the oxidation of phenol into pyrocatechin and hydroquinon (orthobioxybenzol = $\text{C}_6\text{H}_6\text{O}_2$), which for the most part appears in the urine as ethersulphuric acid (*Baumann and others*). [These substances in an alkaline urine become brown on exposure to air, and produce the dark colour of the urine in so-called carbouluria.]

3. Parakresol ($\text{C}_7\text{H}_8\text{O}$), (hydroxyltoluol, with its isomers *ortho*- and *meta*-kresol (the latter in traces), is more abundant in urine (*Baumann, Preusse*). It also occurs in conjugation with sulphuric acid. [It occurs as **kresol sulphate of potassium**, $\text{C}_7\text{H}_7\text{O} \cdot \text{SO}_3\text{K}$.]

Test for phenol (and also kresol):—Distil 150 c.c. urine with dilute sulphuric acid. The distillate gives a brown crystalline deposit of tribromophenol with bromine water, as well as a red colour with Millon's reagent.

Hydroxybenzol (pyrocatechin, hydroquinon) is obtained from urine when it is heated for a long time with hydrochloric acid.

Resorcin, which is an isomer of hydroquinon, when administered internally, also appears in the urine as ethersulphuric acid. Toluol and naphthalin behave similarly. Benzol is oxidised to phenol.

4. Pyrocatechin or Katechol, $\text{C}_6\text{H}_6\text{O}_2$ (metadihydroxybenzol), is formed along with hydroquinon from phenol, and is an isomer of the former. It behaves like

indol and phenol, for when united with sulphuric acid, it yields the pyrokatechin-forming substance. Small quantities sometimes occur in human urine; it is more abundant in the urine of children; it becomes darker when the urine putrefies.

5. **Skatol** [$C_8H_6(CH_3)N$ (methyl-indol)], which is crystalline, and is formed during putrefaction in the intestine, also appears in the urine as a compound of sulphuric acid (§ 252), [*i.e.*, as skatoxyl-sulphate of potassium, $C_8H_8NO \cdot SO_3K$]. On feeding a dog with skatol, Brieger found much potassic skatol-oxy-sulphate.

Test.—Skatol compounds are recognised by adding dilute nitric acid, which causes a violet colour, or fuming nitric acid, which precipitates red flakes (*Nencki*). Its quantity is regulated by the same conditions as indican.

[It is important to notice that the aromatic combinations present in the urine occur as **conjugated sulphuric acid compounds**, *i.e.*, as **etheral sulphates**. Indol, phenol, and skatol, derived from the putrefactive decomposition of proteids in the intestine, must somewhere after absorption unite with sulphuric acid—probably in the liver—to form these compounds, *i.e.*, that in the liver poisonous compounds are converted into innocuous ones (p. 324). Baumann has shown that if the intestine be disinfected, the conjugated sulphuric acid disappears from the urine.]

The **aromatic oxyacids**, **hydroparacumaric acid**, and **paraoxyphenylacetic acid** (the former a putrefactive product of flesh, the latter obtained by E. and H. Salkowski from putrid albumin) occur in the urine (*Baumann*, § 252). **Test.**—Shake the urine treated with a mineral acid with ether, evaporate the latter, and dissolve the residue in water. If aromatic oxyacids are present, they give a red colour with Millon's reagent.

Baumann gives the following series of bodies, which are formed from tyrosin by decomposition and oxidation; most of the substances are formed both during the decomposition of albumin, and also in the intestine, whence they pass into the urine:—Tyrosin, $C_9H_{11}NO_3 + H_2 = C_9H_{10}O_3$ (hydroparacumaric acid) + NH_3 . $C_9H_{10}O_3 = C_8H_{10}O$ (paraethylphenol, not yet proved) + CO_2 . $C_8H_{10}O + O_3 = C_8H_8O_3$ (paraoxyphenylacetic acid) + H_2O . $C_8H_8O_3 = C_7H_8O$ (parakresol) + CO_2 . $C_7H_8O + O_3 = C_7H_6O_3$ (paroxybenzoic acid, not yet proved) + H_2O . $C_7H_6O_3 = C_6H_6O$ (phenol) + CO_2 .

Potassium sulphocyanide, or **thio-cyanate**, derived from the saliva, also occurs in urine. [It passes into the intestine, is absorbed into the blood, and is excreted in the urine.] After acidulation with hydrochloric acid, its presence may be detected by the ferric chloride test (§ 146—*Gscheidlen and J. Munk*). One litre of human urine contains 0.02 to 0.08 gram combined with an alkali.

Succinic acid ($C_4H_6O_4$) occurs chiefly after a diet of flesh and fat, and almost disappears after a vegetable diet. It is a decomposition-product of asparagin, and occurs in considerable amount in the urine after eating asparagus. It is also a product of the alcoholic fermentation (§ 150), and as it passes out of the body unchanged, it occurs in the urine of those who imbibe spirituous liquors. It passes unchanged into the urine (*Neubauer*).

Lactic acid ($C_3H_6O_3$) is a constant constituent of urine. Some observers have found fermentable lactic acid in diabetic urine; sarcolactic acid after poisoning with phosphorus and in trichinosis. Occasionally traces of **volatile fatty acids** are present. Some **animal gum** occurs in urine (p. 476), and Bechamp's "**nephrozymose**" consists for the most part of gum (*Landwehr*). This substance is precipitated from urine by adding to it three times its volume of 90 per cent. alcohol. It is not a simple body, but at 60° to 70° C. it transforms starch into sugar (*v. Wintschan*).

Ferments.—Traces of **diastatic**, **peptic**, and **rennet ferment** have been found, especially in urine of high specific gravity. [Fibrin placed in urine absorbs the ferments.] Trypsin is said not to occur normally (*Leo*).

Traces of **sugar** [*i.e.*, **dextrose**] (*Brücke, Benze Jones*), to the amount of 0.05 to 0.01 per cent., occur in normal urine. [Bunge doubts the occurrence of sugar and lactic acid in normal urine.] After the ingestion of milk-, cane-, or grape-sugar (50 grms.) these varieties of sugar appear in small quantity in the urine (*Worm-Müller*—§ 267, 7).

Kryptophanic acid ($C_3H_9NO_5$), according to Thudichum, occurs as a free acid in urine, but Landwehr regards it as an animal gum.

Reducing substances.—Substances which give Trommer's test always occur in the urine. Normal human urine reduces cupric salts, like a 0.15–0.25 solution of

grape-sugar (more in fever). About $\frac{5}{6}$ of these substances seems to be compounds of glycuronic acid (§ 275), and $\frac{1}{6}$ is due to uric acid and kreatinin (*Flückiger*).

Aceton (C_3H_8O) is formed when normal urine is oxidised with potassic bichromate and sulphuric acid, and it is formed from a reducing substance present in normal urine (apparently derived from the grape-sugar of the blood). Aceton occurs in traces as a normal urinary constituent, which is increased during increased metabolism of the tissues, *e.g.*, carcinoma, inanition. It has also been found in the blood in fever (*v. Jaksch*). **Lieben's Test.**—Acidulate half a litre of urine with HCl and distil; when treated with tincture of iodine and ammonia there is a turbidity due to iodoform (p. 517).

II. THE INORGANIC CONSTITUENTS OF THE URINE.—The inorganic constituents are either taken into the body as such with the food and pass off unchanged in the urine, or they are formed in the body, owing to the sulphur and phosphorus of the food being oxidised and the products uniting with bases to form salts. The quantity of salts excreted daily in the urine is 9 to 25 grams [$\frac{1}{4}$ to $\frac{3}{4}$ oz.].

Sodic chloride—to the amount of 12 (10 to 13) grams [180 grains]—is excreted daily. It is increased, after a meal, by muscular exercise, drinking of water, and generally, when the quantity of urine is increased, by the free use of large quantities of common salt, and by potash salts also; it is diminished under the opposite conditions.

In disease it is greatly diminished; in pneumonia and other inflammations accompanied by effusions, in continued diarrhoea and profuse sweating, constantly in albuminuria and in dropsies. [In cases of pneumonia, sodic chloride may at a certain stage almost disappear from the urine:—*e.g.*, to 1 or 2 grams—at the crisis 8 grams, and the day after 16 grams—and it is a good sign when the chlorides begin to reappear.] In other chronic diseases, the amount of NaCl excreted runs nearly parallel with the amount of urine passed. In conditions of excitement the amount of sodic chloride is diminished, and potassic chloride increased; in conditions of depression the reverse is the case (*Zeulzer*).

Tests for chlorides.—Add to the urine nitric acid and then nitrate of silver solution, which gives a white curdy precipitate of chloride of silver. In albuminous urine the albumin must first be removed. *Microscopically* look for the step-like forms of common salt, and also for the crystals of sodic chloride and urea (§ 256, 4).

[**Estimation of Chlorides** (Volhard's method).—(1) A S.S. (*i.e.*, a standard solution) of silver nitrate is prepared so that 1 c.c. = 0.10 gm. NaCl or 0.06 of Cl. It is placed in a burette. (2) A 10 per cent. solution of neutral chromate of potash is used as the indicator.

Place 2 c.c. of urine in a glass, add a few drops of (2), and drop in (1) from a burette—a red precipitate of chromate of silver, which disappears on shaking, giving place to a white precipitate of silver chloride. Add S.S. until the fluid in daylight retains a red colour, not orange, *i.e.*, until all the chlorine has been precipitated, which is indicated by the persistence of the red colour of the chromate of silver. Read off the number of c.c. of the S.S. used. Multiply the number of c.c. of urine passed by the number of c.c. of S.S. used and divide by 200. Suppose a person passed 2000 c.c. of urine in 24 hours and 2 c.c. of the S.S. were required to obtain the reaction, then $\frac{2000 \times 2}{200} = 20$ grams of NaCl.

Mohr's Method.—This simple method gives approximate results. Dilute 10 c.c. of urine with water to 100 c.c.; neutralise with carbonate of soda, add 3 drops of a concentrated solution of potassic chromate. Drop in from a burette a S.S. of silver nitrate (14.53 grms. to 500 c.c. water), until on stirring a red colour persists. Every c.c. of the S.S. = 10 milligrams of NaCl or 0.06607 grams of chlorine.

2. Phosphoric acid occurs in urine [in the form of two classes of phosphates,—(1) **Alkaline phosphates** as acid sodic phosphate, acid potassic phosphate, and (2) **Earthy phosphates**,—acid calcic and magnesian phosphates to the amount of about 2 grams daily [30 grains]; it is more abundant after an animal than after a vegetable diet. The amount increases after a mid-day meal until evening, and falls during the night until next day at noon. It is partly derived from the alkaline and earthy phosphates of the food, and partly as a decomposition-product of lecithin and nuclein. As phosphorus is an important constituent of the nervous

system, the relative increase of phosphoric acid is due to increased metabolism of the nervous substance.

Pathological.—In fevers, the increased excretion of potassic phosphate is due to a consumption of blood and muscle (§ 220, 3). It is also increased in inflammation of the brain, softening of the bones, diabetes, and oxaluria; after the administration of lactic acid, morphia, chloral, or chloroform. It is diminished during pregnancy, owing to the formation of the fetal bones; also after the use of ether and alcohol, and in inflammation of the kidney.

[Tests.]—To urine add nitric acid and solution of ammonium molybdate and boil, a canary-yellow precipitate of ammonium phosphomolybdate indicates the presence of phosphoric acid. Or, add half its volume of caustic potash to urine, and boil. The earthy phosphates are precipitated, but not the alkaline phosphates.]

Earthy phosphates are precipitated by heat in some pathological urines. This precipitate is distinguished from albumin, which is also precipitated by heat, by being soluble in nitric acid, which precipitated albumin is not. [The earthy phosphates are not precipitated until near the boiling point.]

[Quantitative Estimation of Phosphoric Acid.]—The amount of phosphoric acid is estimated by titration with a *standard solution of uranium acetate*; *ferrocyanide of potassium* being the indicator. The indicator gives a brownish-red colour when there is an excess of free uranium acetate.

Place 50 c.c. of filtered urine in a beaker, add to it 5 c.c. of a solution of sodic acetate (containing 100 grams of sodic acetate and 100 c.c. of acetic acid in 1 litre of water). In a burette place a S.S. of uranium acetate which is previously titrated to such a strength that 1 c.c. = .005 grm. phosphoric acid. Drop in the standard solution, until a drop of the mixture gives a faint brown colour with a drop of the indicator (ferrocyanide of potassium). This is done on a porcelain slab. Boil and test again. If necessary, add a few more drops of the S.S. until the brown colour reappears. Read off the c.c. of the S.S. used. Suppose 17 c.c. of the S.S. are used, then $.005 \times 17 = .085$ grms. phosphoric acid in 50 c.c. urine. Suppose a patient passes 1250 c.c. urine in 24 hours, then $50 : 1250 :: .085 : x$

$$\frac{1250 \times .085}{50} = 2.12 \text{ grams of phosphoric acid passed in 24 hours.}]$$

In addition to phosphoric acid, phosphorus occurs in an incompletely oxidised form in the urine, *e.g.*, glycerophosphoric acid [$C_3H_5PO_3$] (§ 251, 2), which occurs to the amount of 15 milligrams in a litre of urine; it is increased in nervous diseases and after chloroform narcosis.

3. Sulphuric acid occurs in the urine, the greater part in combination with the alkalies, [*i.e.*, as **pre-formed or combined sulphuric acid**], and the remainder united with indol, skatol, and pyrokatechin, in the form of **aromatic ethersulphuric compounds**, *i.e.*, as **conjugated sulphuric acid** (p. 503), [forming the **ethereal sulphates**], the ratio being 1 : 0.1045. All conditions which favour the formation of indol, skatol, or pyrokatechin increase the amount of combined or conjugated sulphuric acid. The total **daily amount** of sulphuric acid is 2.5 to 3.5 grams [37 to 52 grains]. It is increased by the administration of sulphur (*Krause*). The sulphuric acid is chiefly derived from the decomposition of proteids, and hence its amount runs parallel with the amount of urea excreted. The amount of alkaline sulphates in the food is, as a rule, very small.

Test for Sulphuric Acid.—Barium chloride gives a copious white heavy precipitate of barium sulphate, insoluble in nitric acid.

An increased excretion of sulphuric acid in fevers indicates an increased metabolism of the tissues of the body. In renal inflammation it has been observed to be diminished, and in eczema it is greatly increased. Feeding with taurin (which contains sulphur), in the case of rabbits, (but not in carnivora or man), increases the sulphuric acid in the urine (*Salkowski*). According to Zülzer, a copious secretion of bile lessens the relative amount of sulphuric acid in the urine.

In addition to sulphuric acid, sulphur ($\frac{1}{2}$) occurs in an incompletely oxidised form in the urine (potassium sulphocyanide, cystin, and sulphur-bearing compounds derived from the bile) (*Kunkel, v. Voit*—§ 177, 6). *Hyposulphurous acid*, as an alkaline salt, is an *abnormal* constituent in typhus; and so is sulphuretted hydrogen, which is recognised by the blackening of a piece of paper moistened with lead acetate and ammonia, held over the urine.

Quantitative Estimation of Sulphuric Acid.—Acidulate strongly with acetic acid 50 c.c. of urine and add to it an equal volume of water and barium chloride. After being heated for an hour or so in the water-bath, the precipitate falls and is then collected on a filter, and

washed with water, then with dilute HCl, and again with water. The baric sulphate purified in this way is then burned and weighed. It contains all the sulphuric acid which formed salts, *i.e.*, all the combined sulphuric acid.

The filtrate and the washings obtained after the above process contain the sulphuric acid combined with organic bodies. The filtrate and washing are mixed, to them is added $\frac{1}{2}$ of its volume of HCl, and the whole is heated for some time. Barium sulphate and a resinous substance separate out. Filter, dissolve and wash the resinous substance off the filter with hot alcohol, then wash with hot water, dry, and burn the deposit; 1 part barium sulphate corresponds to 0.3433 H_2SO_4 .

[It is important to notice that **sulphur** occurs in several combinations in urine, as the ordinary bibasic salts and the monobasic conjugated sulphuric acid. The latter forms about one-tenth of the average amount of ordinary sulphuric acid. The ordinary sulphates are precipitated, after acidulation, by a soluble barium salt (p. 506). The filtrate still contains conjugated sulphuric acid. Add hydrochloric acid to the filtrate and boil; the conjugated sulphuric acids are broken up and may also be precipitated as a salt of barium. The filtrate from this still contains some sulphur organically combined. Under certain circumstances cystin and sulphocyanides both containing sulphur occur in the urine.]

4. Excessively minute traces of **silicic acid** and **nitric acid** derived from drinking water have been found in urine. *Organic acids*, *e.g.*, citric and tartaric, when taken internally, increase the amount of *carbonates* in the urine. The urine may effervesce on the addition of an acid.

The **sodium** in the urine is chiefly combined with chlorine, but a small part of it is united with phosphoric and uric acids; **potassium** (which is about $\frac{1}{3}$ of the sodium) is chiefly combined with chlorine. In fevers, more potash is excreted than soda, and during convalescence the reverse is the case; **calcium** and **magnesium** exist in normal **acid** urine as chlorides or acid phosphates. If the urine is **neutral**, neutral calcium phosphate and magnesium phosphate are precipitated. Ebstein found the latter in alkaline urine, as large clear four-sided prisms, in diseases of the stomach. If the urine is **alkaline**, calcium carbonate (fig. 338) and tribasic calcic phosphate are deposited as such, while the magnesium is precipitated in the form of ammonio-magnesium phosphate or triple phosphate. The calcium is derived from the food, and depends upon the amount of lime salts absorbed from the intestine. **Free ammonia** is said to occur (0.72 gram or 7 grains daily) in perfectly fresh urine (*Neubauer, Brücke*), and the amount is greater with an animal than with a vegetable diet (*Coranda*). The amount of fixed ammonia is increased by the administration of mineral acids (*Walter, Schmiedeberg, Gäthgens*). **Iron** (1 to 11 milligrams per litre) is never absent. There is a trace of **hydric peroxide** (*Schönbein*), which is detected by its decolorising indigo-solution on the addition of iron sulphate.

Gases.—24.4 c.c. of gas was obtained from one litre of urine—100 volumes of the gases pumped out consisted of 65.40 vol. CO_2 , 2.74 O, 13.86 N. After severe muscular action, the amount of CO_2 may be doubled; digestion also increases it, copious drinking diminishes it.

263. FERMENTATIONS OF URINE.—**Acid Fermentation.**—When perfectly fresh urine is set aside, it gradually becomes more acid from day to day. This is called the “**acid fermentation**.” It seems to be due to the development of special fungi (fig. 316, *a*), and the process is accompanied by the deposition of *uric acid* (*c*), *acid sodium urate*, in amorphous grains (*b*), and *calcium oxalate* (*d*). According to Scherer, the fungus and the mucus from the bladder decompose part of the urinary pigment into lactic and acetic acids. The latter sets free uric acid from neutral sodium urate, so that free uric acid and sodium urate must be formed. *Butyric* and *formic acids* have been found as abnormal decomposition-products of other urinary constituents. When the acid fermentation begins, the urine absorbs

tion may take place within the bladder, when the urine always contains pus-cells (fig. 323) and detached epithelium. When much pus is present, the urine contains albumin. Ammoniacal urine forms white fumes of ammonium chloride, when a glass rod dipped in hydrochloric acid is brought near it. [When ammonia is added to normal urine, triple phosphate is precipitated in a *feathery* form (fig. 341).]

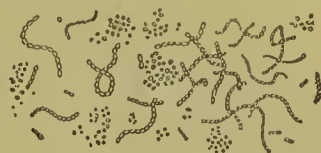


Fig. 318.

Micrococcus ureae.

[Significance of Triple Phosphate.—If urine be alkaline when it is passed, and the alkalinity be due to a *volatile alkali*, i.e., to NH_3 , then decomposition of the urine has taken place, and this kind of urine is a sure sign that there is disease of the genito-urinary mucous membrane.]

264. ALBUMIN IN URINE OR ALBUMINURIA.—Serum-albumin is the most important **abnormal** constituent in urine which engages the attention of the physician. It occurs in blood (§ 32), and its characters are described in § 249. [In some cases, perhaps in most cases, serum-globulin is present along with serum-albumin.]

Causes of Albuminuria.—1. Serum-albumin may appear in urine without any apparent anatomical or structural change of the renal tissues. This condition has been called by v. Bamberger "*Hæmatogenous albuminuria*," and by Leube "*physiological albuminuria*" although the latter term is not a good one. It occurs but rarely, however, and sometimes in healthy individuals when there is an excess of albumin in the blood-plasma (e.g., after suppression of the secretion of milk), and after too free use of albuminous food. 2. As a result of *increased blood-pressure* in the renal vessels, e.g., after copious drinking. It may be temporary or it may be persistent, as in cases of congestion following *heart disease*, emphysema, chronic pleuritic effusions, infiltrations of the lungs, and after compression of the chest, causing congestion in the pulmonary circuit, which extends even into the renal veins, &c. 3. After section or paralysis of the *vaso-motor nerves* of the kidneys, which causes great congestion of these organs. The albuminuria, which accompanies intense and long-continued abdominal pain, is brought about owing to a reflex paralysis of the renal vessels. 4. After violent muscular exercise. [Senator found that forced marches in young recruits were very frequently followed by the appearance of albumin in the urine, which persisted for several days.] *Convulsive disorders*, e.g., epilepsy, the spasms of dyspnoea after strychnin poisoning, in shock of the brain, apoplexy, spinal paralysis, and violent emotions; the excessive use of morphia, which perhaps acts on the vaso-motor centres. 5. It may accompany many acute febrile diseases, e.g., the exanthemata (scarlet fever), typhus, pneumonia, and pyæmia. In these cases it may be due to the increase of temperature paralysing the vessels, but more probably the secretory apparatus of the kidney is so changed (e.g., cloudy swelling of the renal epithelium) that the albumin can pass through the renal membrane. 6. Certain degenerations and inflammations of the kidneys at several of their stages. 7. Inflammation or suppuration in the ureter or urinary passages. 8. Certain chemical substances which irritate the renal parenchyma, e.g., cantharides, carbolic acid. 9. The complete withdrawal of common salt from the food. The albumin disappears when the common salt is given again. 10. The *epithelium* may be in such a condition that it *cannot retain the albumin within the vessels*, due to imperfect nourishment and functional weakness of the excretory elements. This includes the albuminuria of ischæmia, and that after hæmorrhage, in anæmia, scorbutus, icterus, diabetes. [Grainger Stewart finds that albuminuria is more common among presumably healthy people than was formerly supposed.] [11. Besides the experimental conditions mentioned above, what is called experimental albuminuria may be produced by pressure on the renal vein, or by closing the renal artery for a short time and then removing the obstruction and allowing the blood to circulate.]

[Besides being derived from the secreting parenchyma of the kidney, albumin may be present owing to admixture with the secretions from any part of the urinary tract, including the vagina and uterus in the female. In some cases the transudation of albumin is favoured by changes in the capillary walls, the albumin being forced through by the intravascular pressure. Sometimes albuminuria occurs during the course of severe typhoid fever, and in acute fevers generally, where the temperature is persistently above 40°C . (104°F). The high temperature alters the filtering membrane and permits the filtration of albumin.]

[So-called **Physiological Albuminuria**.—This term has been applied to that condition of the urine, where traces of albumin are found in individuals *apparently* in perfect health. Johnson and Pavy cite such cases, while Posner asserts that all urine—even healthy urine—contains traces of proteids, whose presence is ascertained after concentrating the urine. It is safe to assume that normal urine should give no reaction with the usual tests for albumin. Posner precipitated the urine with alcohol, washed the precipitate, dissolved it in acetic acid, and tested it,

with the ferrocyanide test for albumin. He finds that minute traces of proteid are detected by the following modification of the binet test:—Make the urine alkaline, and by the "contact method" bring a layer of very dilute cupric sulphate over it; when the two fluids touch, a reddish-violet ring is obtained.]

The tests for albumin in urine depend upon the facts that it is coagulated by heat in neutral or acid solutions, and it is precipitated by various reagents.

[(1) **Heller's Test.**—Place 10 c.c. of the urine in a test-glass, and pour in pure colourless HNO_3 so as to run down the side of the glass, forming a layer beneath the urine. A white zone of coagulated albumin indicates the presence of albumin. In this test it is important to wait a certain time for the development of the reaction. In urines of high specific gravity, a haziness due to *acid urates* may be formed above where the two fluids meet, but its upper edge is not circumscribed. The acid decomposes the neutral urates and forms a more insoluble acid salt. This cloud of acid urates is readily dissolved by heat, while the albumin is not; the latter is always a sharply defined zone between the two fluids. In very concentrated urine (rare), nitric acid may gradually precipitate *crystalline* urea nitrate. In patients taking copaiba, nitric acid, by acting on the resin, causes a slight milkiness.]

[(2) **Boiling and Nitric Acid.**—Place 10 c.c. of urine in a test-tube and boil. If albumin be present in small quantity, a faint haziness, which may be detected in a proper light, will be produced. Add 10 to 12 drops of HNO_3 . If the turbidity disappears it is due to phosphates, while if any remains it is due to albumin. If albumin be present in large quantity, a copious whitish coagulum is obtained. **Precautions.**—(a) In all cases, if the urine be turbid, filter it before applying any test. (b) *How to boil.*—Boil the upper strata of the liquid, and take care, if any coagulum be formed, that it does not adhere to the side of the tube, else the tube is liable to break. (c) In performing this test with a *neutral* solution, note when the precipitate falls, for albumin is precipitated about 70°C ., phosphates not till about the boiling point. (d) *Amount of Acid.*—If too little (2 or 3 drops) HNO_3 be added, or too much (30 or 40 drops), we may fail to detect albumin, although it is present.]

(3) **Ferrocyanide Test.**—By the addition of *acetic acid* and *potassium ferrocyanide*. [If albumin be present, a white flocculent precipitate separates in the cold. Dr Pavy has introduced *pellets*, consisting of a mixture of citric acid and sodic ferrocyanide. All that is required is to add a pellet to the suspected urine. **Oliver's Papers.**—Dr Oliver uses papers, one saturated with citric acid and another with ferrocyanide of potassium. The two papers are added to the clear filtered urine. Other precipitants of albumin, such as small pieces of paper impregnated with potassio-mercuric iodide, are used by Oliver.]

(4) **Boiling Acid Urine.**—If the urine be alkaline, although albumin may be present, it is not precipitated by heat alone. We require to add acetic acid until a slightly acid reaction is obtained. Boiling may give a precipitate of earthy phosphates in an *alkaline* urine, owing perhaps to the CO_2 being driven off. This precipitate might be mistaken for albumin, but on adding acetic acid or nitric acid, the earthy precipitate is dissolved, while the precipitate of albumin is not dissolved. In testing for albumin, always use *clear* urine. If it is turbid, filter it.

[(5) **Metaphosphoric acid** is dissolved in water just before it is to be used and added to clear urine (*Hindentlang*). Graham pointed out that metaphosphoric acid precipitated albumin. A 20 per cent. solution of the ordinary glacial phosphoric acid is a good test for albumin, but it also precipitates peptones. It, however, changes into ordinary phosphoric acid by keeping, and then it no longer precipitates albumin.]

[(6) **Sodic Sulphate and Acetic Acid.**—Acidulate 10 c.c. of urine with acetic acid, and add $\frac{1}{2}$ of its volume of a concentrated solution of sulphate of soda or magnesia. On heating, if albumin be present, a distinct cloudiness is obtained.]

[(7) In *picric acid* according to Dr Johnson, we have a more delicate test for minute traces of albumin than either heat or nitric acid, or than both these tests combined. It is used either in the form of crystals or powder, or as a saturated aqueous solution. Take a four-inch column of urine in a test-tube, hold the tube in a slanting direction, and pour an inch of the picric acid solution on the surface of the urine, where, in consequence of its low specific gravity (1005), it mixes only with the upper layer of the urine. It coagulates any albumin present. The precipitate occurs at once, and is increased by heat, while the urate of soda, which is sometimes precipitated, is soluble on heating. Peptones and albumoses are also precipitated by this reagent, but the precipitate redissolves on heating.]

[(8) **Potassio-mercuric iodide**, or **Tanret's reagent**, gives a white precipitate. This is a very delicate test, but it also precipitates peptones and albumoses (but these precipitates are dissolved by heat), alkaloids, and bile-salts. The reagent consists of mercuric chloride, 1.35 grams; potassium iodide, 3.32 grams; acetic acid, 20 c.c.; and water, 64 c.c.]

[Dr Roberts regards any test for albumin which requires strong acidulation with an *organic* acid, citric, acetic, or lactic, as unsatisfactory, since it precipitates mucin. For this reason he rejects the tungstate, mercuric iodide, and potassic ferrocyanide tests. Dr Roberts regards the

heat test, with the addition of a small definite quantity of acetic acid, as the best test for the detection of small quantities of albumin.]

1. **Quantitative Estimation** of albumin.—100 c.c. of urine are boiled in a capsule, some acetic acid being ultimately added, whereby the albumin is precipitated in flakes. The precipitate is collected on a weighed, dried (110°), ash-free filter, and repeatedly washed with hot water, then with alcohol, and dried in an air-bath at 110° . The weight of the filter is deducted, and finally the dried filter with the albumin is burned in a weighed platinum capsule, and the weight of the ash also deducted. [This method is not available for the busy practitioner on account of the time it takes. Practically, it is sufficient to compare from day to day the proportion that the precipitated albumin bears to the bulk of the urine tested. A graduated tube may be used, so that after the precipitate has subsided, the physician may see what proportion of the whole the precipitate occupies.]

Esbach's Albuminometer (fig. 319).—A glass cylinder is filled with the urine up to the mark U, and to R with the precipitant (20 citric acid, 10 picric acid, 970 water). The vessel is corked and turned upside down several times to secure the mixture of the fluids. After twenty-four hours the coagulated albumin subsides, when the graduation on the tube indicates the number of grams of albumin per 1000 c.c. of urine. Very albuminous urine must be previously diluted. [Suppose the amount of deposit to reach to 3, and the patient passed 1800 c.c. of urine in 24 hours, the amount of albumin is $1.8 \times 3 = 5.4$ grams in 24 hours. That is, 3 grams in 1000 c.c., therefore $\frac{1800 \times 3}{1000} = 5.4$.]

2. **Serum-globulin** occurs only in albuminous urine, and is frequently present. Its presence is ascertained by [neutralising and] adding powdered magnesium sulphate in excess to the urine; when it is present it is precipitated (§ 32). The more globulin there is in the presence of albumin, the more difficult it is to precipitate it. Sometimes, when an albuminous urine is dropped into a large cylinder of water, each drop as it sinks is followed by a milky train, and when a sufficient number of drops have been added, the water becomes opalescent, the opalescence disappearing on adding an acid. The globulin is kept in solution by common salt and other neutral salts, but when these are largely diluted, the globulin is precipitated (*Roberts*).

3. **Peptone** occurs in some specimens of albuminous urine, but also in non-albuminous urine. Maixner found it constantly in the urine in all cases where suppuration is present, and even in phthisis, constituting **pyogenic peptonuria**. Peptone occurs in pus, and the **peptonuria** in these cases is a sign of the breaking up of the pus-cells (*Hofmeister*). Also when many leucocytes are broken up in the blood (**hæmatogenic**). It occurs in cases where there is great disintegration of albuminous tissues, *e.g.*, in cancer, [suppurative diseases, empyema, croupous pneumonia, phosphorus-poisoning, &c.]. It is frequently found after child-birth. Ammonium sulphate precipitates all proteids except peptones (p. 464).

[The only satisfactory test for peptone is to precipitate all the other proteids with ammonium sulphate, and any proteid remaining in solution in the filtrate must then be peptone. Many of the so-called cases of peptonuria (*Martin*) (in suppurative diseases) are really due to the presence of deuto-proteose. This last substance gives all the reactions for peptone except the following two. It is precipitated by ammonium sulphate, while peptone is not. It gives no precipitate with nitric acid unless a considerable amount of salt is added, and this precipitate disappears on heating and reappears on cooling, while peptone gives no precipitate with nitric acid.]

[When peptone is injected into the blood it is excreted in the urine as peptone (p. 36). Deuto-albumose similarly injected appears as peptone.]

Test.—Separate the albumin by boiling and the addition of acetic acid. Treat the filtrate with three volumes of alcohol; this precipitates the peptone, which, when dissolved in water, gives the characteristic reactions for peptone (§ 166, 1.).

4. **Proteoses**, *i.e.*, **Hemialbumose** or **propeptone** occur very rarely, *e.g.*, in osteomalacia and intestinal tuberculosis (*Bence Jones*). The urine is heated to saturation with NaCl and a large quantity of acetic acid added, and filtered while hot, to separate the albumin and globulin. In the cold filtrate hemialbumose forms a turbidity, which is redissolved by heat. The precipitate thrown down by HCl and HNO_3 is soluble by heat (*Kühne*). The precipitate is isolated by filtration, and dissolved in a little warm water, when it gives with HNO_3 a yellow reaction; like peptone the solution gives the biuret-reaction (p. 466). [Another proteose occurring in the urine is **deuto-proteose**, which has been mistaken for peptone (see above).]

5. **Egg-albumin** appears in the urine when much egg-albumin is taken in the food, and also when it is injected into the blood-vessels (§ 192, 4). According to Seminola, the albumin present in the urine in Bright's disease has undergone a molecular change (similar to egg-albumin), and hence it is excreted.



Fig. 319.

Esbach's albuminometer.

6. **Mucus** is present in large amount, especially in catarrh of the bladder. It contains numerous mucous corpuscles, which are scarcely distinguishable from pus corpuscles. They contain albumin, so that urine containing much mucus is albuminous; mucin is not precipitated by heat, but acetic acid gives a flocculent precipitate in clear urine. [Minute traces of mucin occur normally in urine. If clear normal urine be set aside for a short time, a flocculent haziness, like a cloud of cotton wool, is seen floating in the urine. This is mucus entangling a few epithelial cells from the genito-urinary tract. **Mucin Reaction.**—According to W. Roberts, the addition of a concentrated solution of citric acid to urine, as in Heller's test (§ 264, a), where the two fluids meet, causes an opalescent zone gradually to be formed above the layer of acid.]

265. BLOOD (HÆMATURIA) AND BLOOD-PIGMENT (HÆMOGLOBINURIA) IN THE URINE.—I. Source of the Blood.—(1) In hæmaturia, the blood may come from any part of the urinary apparatus.

1. In hæmorrhage from the **kidney**, the amount of blood is usually small and well mixed with the urine. The presence of "blood-cylinders," long microscopic blood coagula, casts of the miniferous tubules, washed out of them by the urine, is characteristic when they are found in the urine (fig. 332). The urine usually has a **smoky** appearance. [The urine slowly dissolves out the colouring matter, the stroma of the corpuscles after a time being deposited as a brownish sediment. The smoky hue occurs only in acid urine; if the urine becomes alkaline, the hue becomes brighter red.] The blood-corpuscles show peculiar changes of form, [they become crenated] (fig. 320), and exhibit evidence of division, due to the action of urea on them (§ 5).



Fig. 320.

Fig. 321.

Fig. 320.—Crenated red blood-corpuscles in urine, $\times 350$. Fig. 321.—Peculiar changes of the red blood-corpuscles in renal hæmaturia.

Large coagula are never found in urine mixed with blood derived from the kidney. 2. In hæmorrhage from the **ureter**, we occasionally find worm-like masses of clotted blood, casts of the canal of the ureter. 3. The relatively largest coagula occur in hæmorrhage from the **bladder**. In all cases where blood is present, we must examine microscopically for the blood-corpuscles, and it may be for coagula of fibrin. In acid urine, blood-corpuscles, but never arranged in rouleaux, may be found after two or three days. The blood-corpuscles settle as a red sediment at the bottom. If the hæmorrhage is copious, many retain their original shape, but if the urine is very concentrated, they may become crenated.

When there is a small and slow hæmorrhage from ruptured small capillaries, the red blood-corpuscles are of unequal size, many $\frac{1}{2}$ to $\frac{3}{4}$ the size of normal, while the pigment has become brownish-yellow (fig. 321).

If a hæmorrhage of this kind be accompanied by **catarrhal inflammation of the bladder**, there is found between the red, numerous shrivelled leucocytes (fig. 321), which in freshly passed urine often exhibit lively amoeboid movements. If the urine be alkaline, as it usually is, crystals of triple phosphate also occur.

If the remains of the red blood-corpuscles become very pale, their presence may be frequently ascertained by adding iodine in a solution of KI (fig. 321). Blood is constantly present in the urine during menstruation.

II. Hæmoglobinuria is quite distinct from hæmaturia. It depends upon the excretion of **hæmoglobin as such** through the kidneys, and it is produced when hæmoglobin occurs free within the blood-vessels, as in cases where the coloured blood-corpuscles have been dissolved inside the blood-vessels (hæmocytolysis).

It occurs when foreign blood is transfused, *e.g.*, when lamb's blood is transfused into man. The foreign blood-corpuscles are dissolved in the blood of the recipient, and the hæmoglobin appears in the urine (§ 102). In addition, microscopic "**cylinders**," or "**casts**," consisting of a globulin-like body, tinged yellow with hæmoglobin, may likewise be found in the urine. It also occurs in cases of severe burns (§ 10, 3); after decomposition of the blood in pyæmia, scorbutus, purpura, severe typhus, after respiring arseniuretted hydrogen, and after the passage of azobenzol, naphitol, pyrogallie acid, potassic chlorate, chloral, phosphorus, or carbolic acid into the circulation. [The injection of laky blood, water, ether, glycerin (*Adams*), or toluylendiamin (*Affanassiev*), also causes it, and in such cases Affanassiev asserts that the Hb passes out through the glomeruli, while brown degeneration-products of the red blood-corpuscles, which are dissolved by these agents, were found in the convoluted tubules.] These substances dissolve the red blood-corpuscles. Sometimes it occurs **periodically** from causes and conditions as yet but little understood, *e.g.*, the application of cold to the skin. [In **paroxysmal hæmoglobinuria**, which occurs during periodic febrile attacks, hæmoglo-

bin may be present in the urine, but generally there is also methæmoglobin, which does not seem to be due to the action of the urine on the pigment, but the methæmoglobin seems to be secreted as such in the kidney.]

Tests for Blood in Urine.—1. The colour of bloody urine shows every tint, from a faint red to a dark blackish-brown, according to the amount of blood present. The urine is often turbid.

2. Urine containing blood or blood-pigment contains albumin.

3. **Heller's Blood Test.**—Add to urine half its volume of solution of caustic potash, and heat gently. The earthy phosphates are precipitated, and they carry the hæmatin with them, falling as garnet-red flocculi. [This is not a reliable test.]

4. **Hæmin Test.**—The coloured earthy phosphates may be collected on a filter, and from them hæmin may be prepared as directed in § 19.

5. **Almen's Test.**—Add to urine, freshly prepared tincture of guaiacum and ozonised ether; a blue colour indicates the presence of blood (§ 37).

6. **Spectroscope** (see § 14). Fig. 324 shows the arrangement of the apparatus. The urine is placed in a glass vessel, D, with parallel sides, 1 centimetre apart (hæmatinometer). Light from a lamp, E, passes through the fluid. The lamp, F, illuminates the scale, which is seen by

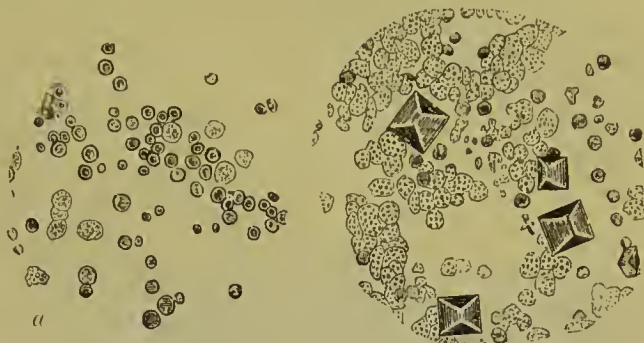


Fig. 322.

Fig. 323.

Fig. 322.—Colonred and (a) colourless blood-corpuscles of various forms. Fig. 323.—Shrivelled blood-corpuscles in urine (catarrh of the bladder), with numerous lymph-corpuscles, and crystals of triple phosphate, $\times 350$.

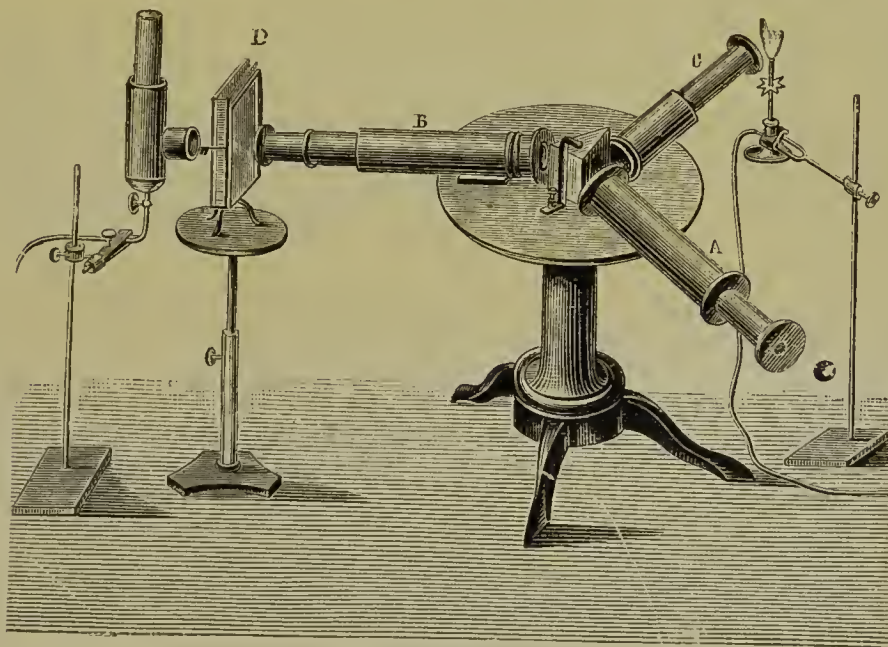


Fig. 324.

Spectroscope for investigating the presence of hæmoglobin in urine.

the observer through the telescope, A. (a) Fresh urine containing blood gives the spectrum of oxyhæmoglobin (fig. 23). (b) When bloody urine is exposed for some time, especially in a warm place, it becomes more acid, and assumes a dark brownish-black colour. The hæmoglobin becomes changed into methæmoglobin (§ 15). It is precipitated by lead acetate, which does not precipitate oxyhæmoglobin; the spectrum of methæmoglobin resembles that of hæmatin in an acid solution (§ 15, fig. 23). The spectra may be combined. (c) The microscopic investigation must never be omitted. The shape of the corpuscles may vary considerably (figs. 320–322).

266. BILE IN URINE (CHOLURIA).—The physiological conditions which cause the bile constituents to appear in the urine are mentioned in part at § 180.

Hæmatogenic or Anhepatogenic Icterus (Quincke), occurs when bilirubin (§ 20) is formed from extravasated blood by the action of the connective-tissue corpuscles, so that bile pigments, in addition to colouring the tissues, pass into the urine.

I. Bile Pigments.—Their presence is ascertained by **Gmelin-Heintz's test.** *Green* (Biliverdin) is the characteristic hue in the play of colours obtained with this test, which is fully described in § 177.

Modifications of the Test.—1. If icteric urine be filtered through filtering or blotting paper, a drop of nitric acid containing nitrous acid, when applied to the inner surface of the spread-out filter, gives a yellowish-coloured ring (*Rosenbach*). 2. In order that the reaction may not take place too rapidly, add a concentrated solution of sodic nitrate, and then slowly pour in sulphuric acid (*Fleischl*). 3. On shaking 50 c.c. of icteric urine with 10 c.c. of chloroform, the bilirubin is dissolved by the latter. On adding bromide water, a beautiful ring of colours is obtained (*Maly*). If the chloroform extract be treated with ozonised turpentine and dilute caustic potash, a green colour, due to biliverdin, occurs in the watery fluid (*Gerhardt*).

[Maréchal's Test.]—Pour tincture of iodine (B.P.) on the surface of the urine in a test-tube. A green colour appears if bile pigments are present.]

In slight degrees of jaundice, **urobilin** alone may be found (§ 261, 1) (*Quincke*).

In persistent high fever, the urine contains especially **biliprasin** (*Huppert*). If it contains **choletelin** alone, add to the urine some hydrochloric acid, and examine it with the spectroscope, which gives a pale absorption-band between *b* and *F* (§ 177, 3, *f*).

Hæmatoidin.—Sometimes crystals of *hæmatoidin* (§ 20, fig. 27) appear in the urine, especially when blood-corpuscles are dissolved within the blood-stream; occasionally in scarlet fever and typhus, and sometimes in cases of periodic hæmoglobinuria. The breaking up of old blood-clots in the urinary passages, as in pyonephrosis (*Ebstein*), or the dissolution of necrotic areas (*Hofmann and Ullmann*) produces them, and similar crystals occur in analogous cases in the sputum (§ 138). In jaundice due to congestion (§ 180), the identical crystalline substance, bilirubin, is found.

II. Bile acids occur in largest amount in absorption jaundice, but they are never present to any extent. The test is described at § 177, 2, the cane-sugar solution consisting of 0.5 gm. to 1 litre of water. If the urine be dilute, it is advisable to concentrate it on a water-bath. [It is rare to get a satisfactory result with Pettenkofer's test in ordinary icteric urine.] V. Pettenkofer's test may be used with the alcoholic extract of the nearly dry residue, but no albumin must be present. Dragendorff found 0.8 gm. in 100 litres of *normal* urine.

Strassburg's Modification.—Dip filter paper into the urine, to which a little cane-sugar has been added; dry the paper and apply to it a drop of sulphuric acid. A violet-red colour is obtained after a short time. **[Hay's Reaction** (§ 177). Icteric urine precipitates the albumin in a solution of acid-albumin (§ 181 G.).]

267. SUGAR IN URINE (GLYCOSURIA).—**Diabetes Mellitus.**—The excessively minute trace of **grape-sugar** or **dextrose**, which is constantly present in normal urine, sometimes becomes greatly increased and constitutes the conditions of **diabetes mellitus** and **glycosuria**. The physiological conditions which determine this result are given at § 175. In this condition, the **quantity of urine** is greatly increased; it may reach 10 or more litres. Many pints may be passed daily. [The usual abnormal amount of sugar is from 1 to 8 per cent., although 15 per cent. has been found, *i.e.*, from 5 to 50 grs. per fluid oz., or 300 to 3000 grs. in twenty-four hours.] The **specific gravity** is also increased (1030 to 1040). [In a case where a large amount of urine is passed of a *pale* colour and a specific gravity above 1030, always suspect sugar.] A diabetic person gives off relatively more water by the kidneys and less by the skin (and lungs?) than a healthy person. The **colour** is very pale yellow, although the amount of pigment is by no means diminished—it is only diluted [the depth of the colour being inversely as the quantity passed]. The amount of the nitrogenous urinary excreta is increased. The sugar is increased by a diet of carbohydrates and diminished by an albuminous diet. The uric acid and oxalate of lime are often increased at the commencement of the disease, while yeast cells are constantly present after the urine has been exposed to the air for some time.

[In **diabetes insipidus** there is a very copious secretion of watery urine without the presence of sugar. It may be produced experimentally by injury to a certain part

of the floor of the fourth ventricle, and it occurs as a diseased condition. It seems to depend on some derangement of the central vaso-motor apparatus of the kidney.]

Sugar has been found *occasionally* [i.e., transitory glycosuria] after poisoning with or after the use of morphia, CO, chloral, chloroform, curare (?) (p. 517); after the injection of ether and amyl-nitrite into the blood; and in gout, intermittent fever, cholera, cerebro-spinal meningitis, hepatic cirrhosis, and cardiac and pulmonary affections.

[There is no doubt that normal healthy human urine contains one or more reducing agents, which reduce cupric oxide to the same extent as if the urine on an average contained 6 grains of glucose in every 10 fluid ounces of urine, or 1.34 grms. per litre. As this substance does not cause alcoholic fermentation in its solutions, its identity with glucose appears to be doubtful. The most active reducing agent is probably kreatinin (*G. S. Johnson*). But Fehling's solution is also reduced by uric acid, hippuric acid, pyrocatechin, and glycuronic acid (p. 517). The only way to distinguish these from dextrose is the fermentation-test. None of them ferment with yeast to yield alcohol and CO₂.]

Tests for sugar.—Any of the tests described at § 149 may be used, but the urine must be free from albumin. The quantitative estimation by fermentation and the titration methods are described in § 149. [The tests for grape-sugar described in § 149 are (1) Trommer's; (2) Fehling's; (3) Moore & Heller's; (4) Böttger's; (5) Mulder & Neubauer's; (6) Fermentation test; (7) Molisch's test.]

8. **Worm-Müller** recommends the following modification of Fehling's test:—Use a 2.5 per cent. solution of cupric sulphate solution, and another of 10 parts of sodio-potassic tartrate in 100 parts of 4 per cent. solution of soda. Boil 5 c.cm. of urine in a test-tube, while in a second test-tube is boiled 1 to 3 c.cm. of the copper solution and 2.5 c.cm. of the potassic-tartrate solution. The boiling of both fluids is stopped simultaneously, and after 20 to 25 seconds the contents of one test-tube are added to those of the other, but without shaking the mixture, the reduction taking place spontaneously.

9. **Nylander's** modification of Böttger's test is also good (§ 149).

[10. **Picric Acid and Potash Test.**—Braun showed that grape-sugar, when boiled with picric acid and potash, reduces the yellow picric acid to the deep red picramic acid, the depth of the colour depending on the amount of sugar present. Dr Johnson uses this test for detecting the presence of sugar in urine, and also for estimating the amount of sugar present, the depth of the red colour obtained on boiling being compared with a standard dilution of ferric acetate. In doing the test, use 1 drachm of urine, $\frac{1}{2}$ a drachm of liquor potassæ, and 10 minims of picric acid solution; make up to 2 drachms with distilled water, and boil the mixture for one minute. This test indicates the presence of 0.6 grain of sugar per fluid ounce of normal urine. Dr Johnson claims for this test that it possesses all the advantages of the other tests, while it is not affected by uric acid or any other normal ingredient of urine; neither does the presence of albumin interfere with the action of the test as it does with all the forms of copper testing.]

[11. **Indigo-carmin Test.**—A blue solution of this substance, when boiled with diabetic urine containing sodic carbonate, changes from a blue to a violet, purple, red, yellow, and finally, straw-yellow colour. After cooling and exposure to the air, the various colours are obtained in the reverse order until the mixture becomes blue again. Dr Oliver uses this test in the form of test-papers. One bibulous paper is impregnated with the indigo-carmin and the other with sodic carbonate. Drop one of the test-papers and a sodic carbonate paper into a test-tube containing 1½ inch of water, heat gently, when a blue solution is obtained. Add the urine slowly, one drop at a time, and boil the mixture, observing any change of colour by holding the tube against a white surface below the level of the eye. Uric acid and urates, which reduce Fehling's solution, do not affect the carmin test, nor does kreatinin, although it reacts with the picric acid test.]

[12. **Phenyl-hydrazin Test.**—It depends on the fact that glucose forms with phenyl-hydrazin a characteristic body, **phenyl-glucosazon**, which takes the form of yellow needles, and is but little soluble in water. Two parts of phenyl-hydrazin chloride and three of sodic acetate are placed together in a test-tube containing 6–8 c.c. urine, and the test-tube is placed for 20–30 minutes in boiling water. After this the tube is put into a vessel containing cold water. If sugar be formed, a yellow deposit separates, which, when

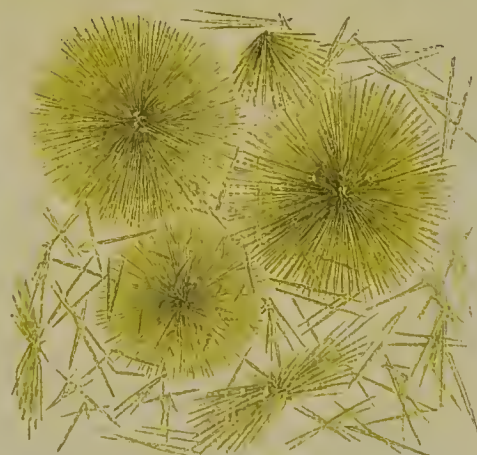


Fig. 325.

Phenyl-glucosazon crystals from urine containing sugar.

examined with the microscope, is seen to consist of crystals of phenyl-glucosazon, either detached or arranged in clusters (fig. 325). The substance melts at 205°C . Albumin, if present, should be got rid of previously.

[Quantitative Estimation of Sugar.—(a) Fermentation Test (§ 150). Take 4 oz. (120 c.c.) of the urine; add a lump of German yeast, about the size of a walnut, lightly cork the bottle, and place it aside for twenty-four hours in a moderately warm place, *e.g.*, on the mantelpiece. Take the specific gravity before and after the fermentation. Thus, if the specific gravity be 1038 before and 1013 afterwards, the difference or “density lost” is 25, which gives 25 grs. of sugar per fluid oz. (*Roberts*). If it be desired to get the percentage, multiply the density lost by 0.23, thus $25 \times 0.23 = 5.69$ in 100 parts.]

[(b) Volumetric Analysis of Sugar.—10 c.c. of Fehling’s solution = .05 gram of sugar.

1. Ascertain the quantity of urine passed in twenty-four hours. 2. Filter the urine, and remove any albumin present by boiling and filtration. 3. Dilute 10 c.c. of Fehling’s solution with about twenty times its volume of distilled water, and place it in a white porcelain capsule on a wire gauze support under a burette. (It is diluted because any change of colour is more easily observed.) 4. Take 5 c.c. of the urine, and 95 c.c. of distilled water, and place the diluted urine in a burette. 5. Gradually boil the diluted Fehling’s solution, and whilst it is boiling gradually add the diluted urine from the burette, until all the cuprous oxide is precipitated as a reddish powder, and the supernatant fluid has a straw-yellow colour, not a trace of blue remaining. Read off the number of c.c. of *dilute* urine employed. Say 36 c.c. were used—that, of course, represents 1.8 c.c. of the original urine. Suppose the patient passes 1550 c.c.; as 1.8 c.c. of urine reduced all the cupric oxide in the 10 c.c. of Fehling’s solution, it must contain .05 gram sugar, hence,

$$1.8 : 1550 :: .05 : \frac{1550 \times .05}{1.8} = 237.5 \text{ grams of sugar passed in 24 hours.}]$$

[Preparation of Fehling’s Solution.—34.64 grams of pure crystalline cupric sulphate are powdered and dissolved in 200 c.c. of distilled water; in another vessel dissolve 173 grams of Rochelle salts in 480 c.c. of pure caustic soda, specific gravity 1.14. Mix the two solutions, and dilute the deep-coloured fluid which results to 1 litre. *N.B.*—Fehling’s solution ought not to be kept too long; it is apt to decompose, and should therefore be preserved from the light, or protected with opaque paper pasted on the bottle. Some other substances in urine, *e.g.*, urates and uric acid, reduce cupric oxide.]

(c) According to Worm-Müller, the polarization method is almost valueless for diabetic urine.

[Picro-Saccharimeter.—G. Johnson uses a stoppered bottle 12 inches long and $\frac{3}{4}$ inch wide, graduated in $\frac{1}{10}$ ths and $\frac{1}{100}$ ths (fig. 326). To it is fixed a shorter bottle containing the standard iron-solution for comparison, a standard solution, composed of liquor ferri perchloride 3j, liq. ammon. acetatis 3iv, glacial acetic acid 3iv, liq. ammoniæ 3i, and water to make up 3iv. All B.P. preparations give a colour identical with a solution containing 1 gr. of grape-sugar per oz., reduced by picric acid and afterwards diluted four times, so that this tint = $\frac{1}{4}$ gr. of sugar per oz. After reducing the sugar with the picric acid, pour into the tall tube the dark saccharine liquid produced by boiling to occupy ten divisions of the tube, and add distilled water cautiously until the colour approaches that of the standard; read off the level of the fluid. The amount of sugar present is determined from the amount of water added. In making the test, the picric acid must be added in proportion to the amount of sugar present.]

If large quantities of dextrose are taken in the food, a part of it (and more in diabetic persons) appears in the urine. Lævulose, when taken internally, does not increase the amount of sugar in diabetes. The free use of starch does not cause glycosuria in health, but in diabetes it increases the amount of sugar. A large consumption of cane- or milk-sugar causes the passage of small quantities of both of these sugars into the urine in health, while in diabetes the amount of dextrose is increased (*Worm-Müller*). According to Külz, in diabetic persons cane-sugar splits up into grape- and fruit-sugar, the latter being used up in the body, and the former partly excreted; and the same is the case with milk-sugar.

In severe cases of diabetes mellitus, Külz found the left-rotatory β -oxybutyric acid (the next highest analogue of lactic acid) in the urine, from which acetic acid is formed by oxidation (§ 175), which in its turn readily yields CO_2 and aceton. α -crotonic acid is formed in urine by the removal of water from oxybutyric acid in the urine in diabetes (*Stadelmann*).

The administration of aceton causes albuminuria, and this may in part explain in some cases the complication of albuminuria in diabetes (*Albertoni and Piseni*).

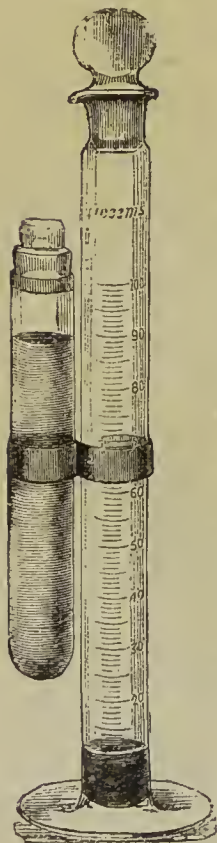


Fig. 326.
Picro-saccharimeter
of G. Johnson.

[Glyconic acid ($C_6H_{10}O_7$) occurs in such excessively small quantities in normal urine that it may be regarded as absent. It is the substance which above all others is most liable to be mistaken for sugar (p. 515). The other substances mentioned on p. 515 which reduce Fehling's solution, do so only to a small extent, but glyconic acid does so like dextrose. It occurs in the urine in large amount after the administration of chloroform, chloral, butyl-chloral, curare, and morphia. It, however, does not undergo the alcoholic fermentation. Ashdown has recorded a case in which it appeared in the urine without any drugs being administered.]

Aceton [C_3H_6O] or Aceton-yielding substance, probably aceto-acetic acid, is sometimes found in diabetic urine. It has a peculiar vinous odour, and it has been detected in the urine during fever. Gerhardt described a peculiar substance in diabetic urine, which gave a deep red colour with perchloride of iron. This substance is probably ethyl-diacetic ether [$C_6H_{10}O_3$], and he considered it to be the source of aceton; but it is more probably derived from aceto-acetic acid. [This substance has been confounded with aceton, but the iron test distinguishes them.] **Tests for Aceton.**—(1) Perchloride of iron = Burgundy-red colour; but this is not reliable. (2) Lieben suggested an iodoform test. Dissolve 20 grains of KI in a fluid draehm of liq. potassæ, and boil the fluid. Pour the suspected urine on the surface, when a ring of phosphates is deposited from the urine by the hot alkaline solution. If aceton be present after a time the deposit becomes yellow, and yellow granules of iodoform appear and sink to the bottom of the test-tube. The only other substance which may be met with in the urine giving this reaction is lactic acid.

Milk-sugar is sometimes found in the urine of women who are nursing; when the secretion of milk is arrested, absorption taking place from the breasts (*Kirsten, Spiegelberg*). **Lævulose** is sometimes found in diabetic urine (§ 252).

Dextrin has also been found in diabetic urine. **Inosit**, or muscle-sugar (§ 252), is sometimes found in diabetes, in polyuria, and albuminuria. It is found in traces even in normal urine. Occasionally, after the pique in animals (§ 175), inosit, instead of grape-sugar, appears in the urine (fig. 327). In testing for inosit, remove the grape-sugar by fermentation, and the albumin by heat after the addition of a few drops of acetic acid and sodie sulphate. Some of the filtrate is evaporated nearly to dryness on a capsule. To the residue add two drops of mercuric nitrate (Liebig's titration fluid for urea), which gives a yellow precipitate. When this coloured residue is spread out and carefully heated, a dark red colour, which disappears on cooling is obtained (*Gallois, Kütz*). Inosit gives a green when boiled with Fehling's solution.]

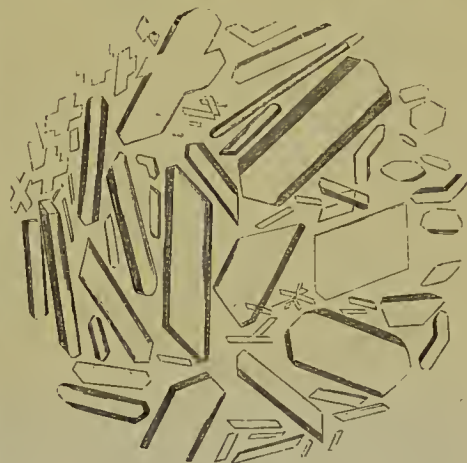


Fig. 327.

Inosit crystallised partly from alcohol and partly from water.

[**Diazo-reaction** or **Ehrlich's reaction.**—This reaction is never given by normal urine, but it is given by the urine in typhoid fever (*Rutimeyer*), acute tuberculous, &c. Its exact clinical significance is unknown. Two solutions are required—(1) a concentrated solution of sulphanilic acid, and (2) a solution of sodium nitrate (1 in 200). 200 c.c. of (1) are mixed with 10 c.c. of pure HCl and 6 c.c. of (2). Mix equal quantities of this mixture and urine rendered strongly alkaline with ammonia; a bright earmine red constitutes the reaction. After standing 24–36 hours a deposit, green or black, on its upper surface occurs.]

268. CYSTIN = $C_6H_{12}N_2S_2O_4$ —This left-rotatory body occurs very seldom in large amount in urine, although it seems to be a constituent of normal urine. It may be in solution or in the form of hexagonal crystals (fig. 328, A) [the latter only in acid urine]. It is insoluble in water, alcohol, and ether, but easily soluble in ammonia, from which solution it may be crystallised. According to Baumann and Preusse, there are intermediate products of the metabolism, from which are furnished the materials necessary for the formation of cystin. During normal metabolism these materials undergo further changes, and the sulphur appears oxidised in the urine as sulphuric acid. In rare cases these oxidations do not take place, and then the sulphur appears in the cystin of the urine (*Stadthagen*). Cystin is increased in phosphorus-poisoning (*Baumann*).

269. LEUCIN = $C_6H_{13}NO_2$. **TYROSIN** = $C_9H_{11}NO_3$.—Both bodies occur in the urine in **acute yellow atrophy of the liver**, and in poisoning by phosphorus. (Their formation during pancreatic digestion has been referred to in § 170, II.) As the urea excreted is usually diminished at the same time, it is assumed that, in these diseases, the further oxidation of the derivatives of the proteids is interfered with. **Leucin**, which is either precipitated spontaneously or obtained after evaporating an alcoholic extract of the concentrated urine, occurs in the form of **yellowish-brown balls** (fig. 329, *a, a*), often with concentric markings, or with fine spines on their surface. When heated it sublimes without fusing.

Tyrosin forms silky **colourless sheaves of needles** (fig. 329, *b, b*). When boiled with mercuric nitrate and nitric acid it gives a red colour, and afterwards a

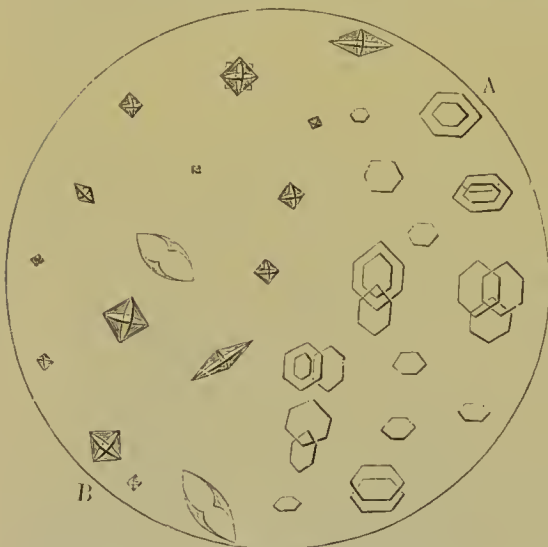


Fig. 328.

A, crystals of cystin ; B, oxalate of lime ;
c, hour-glass forms of B.



Fig. 329.

a, a, leucin balls ; *b, b*, tyrosin sheaves ;
c, double balls of ammonium urate.

brownish-red precipitate. **Piria's Test**.—When slightly heated with a few drops of concentrated sulphuric acid, it dissolves with a temporary deep red colour. On diluting with water, adding barium carbonate until it is neutralised, boiling, filtering, and adding dilute ferric chloride, a violet colour is obtained (*Piria, Stüdeker*).

270. DEPOSITS IN URINE.—Deposits may occur in normal and in pathological urine, and they may be either "**organised**" or "**unorganised**."

I. Organised Deposits.

A. Blood : red and white blood-corpuscles and sometimes fibrin (figs. 320–322).

B. Pus, in greater or less amount in catarrh or inflammation of the urinary passages. Pus cells exactly resemble colourless blood-corpuscles (figs. 14, 323). **Donné's Test**.—Pour off the supernatant fluid and add a piece of caustic potash to the deposit ; if it be pus it becomes gelatinous, ropy, and more viscid (alkali-albuminate). **Mucus**, when so acted on, becomes more fluid and mixed with flocculi.

C. Epithelium of various forms occurs, but it is not always possible to say whence it is derived.

D. Spermatozoa may be present.

E. Lower organisms occur in the urinary passages very seldom, but they may be present, *e.g.*, in the bladder, when germs are introduced from without by means of a dirty catheter. [Before introducing a catheter into the bladder one ought always to make sure that the instrument is perfectly aseptic.] Micrococci are found in the urine in certain diseases, *e.g.*, diphtheria. The following forms are distinguished :—

1. *Schizomycetes* (§ 184). *Normal* human urine contains neither schizomycetes nor their spores. In pathological conditions, however, fungi may pass from the blood into the urinary tubules and thus reach the urine (*Leube*). During the alkaline fermentation of urine, micrococci, rod-shaped bacteria or bacilli (fig. 330) appear. *Sarcinæ* belong to the group (§ 186).

2. *Saccharomycetes* (fermentation fungi): (*a*) The fungus of the acid urine fermentation (*S. urinae*) consists of small bladder-like cells arranged either in chains or in groups (figs. 316, *a*; 330, *f*). (*b*) Yeast (*S. fermentum*) occurs in diabetic urine, as oval cells with a dotted eccentrically-placed nucleus (fig. 292).

3. *Phytomycetes* (moulds) occur in putrid urine (fig. 330, *e*). They are without clinical significance.

F. Tube casts.—The occurrence of tube casts, *i.e.*, casts of the uriniferous tubules (*Henle*, 1837), is of great importance in the diagnosis of renal diseases. If these structures are relatively thick and straight, they probably come from the collecting tubules, but if they are smaller and twisted, they probably come from the convoluted tubules. There are various forms of tube casts:—

1. **Epithelial casts**, consisting of the actual cells of the uriniferous tubules. They indicate that there is no very great change going on, but only that, as in catarrhal inflammation of any mucous membrane, the epithelium is in process of desquamation. 2. **Hyaline casts** (fig. 337) are quite clear and homogeneous, usually long and small; sometimes they are “finely granular,” from the presence of fat or other particles. They are best seen after the addition of a solution of iodine. They are probably formed from albumin, which passes into the uriniferous tubules. They are dissolved in alkaline urine, while acid urine favours their formation. They usually occur in the late stages of renal disease, after the tubular epithelium has been shed. 3. **Coarsely granular casts** (fig. 336) are brownish-yellow, opaque, and granular, usually broader than 2. There are various forms. Not unfrequently there are fatty granules, and, it may be, epithelial cells in them. 4. **Amyloid casts** occur in amyloid degeneration of the kidneys (fig. 337). They are refractive and completely homogeneous, and give a

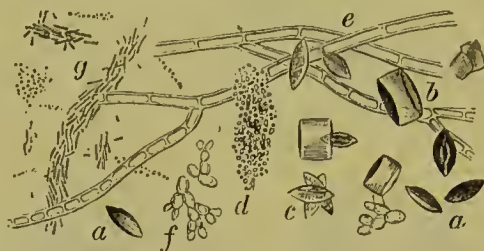


Fig. 330.

Fungi in urine. *e*, mould; *f*, yeast; *d*, *g*, micrococci and bacilli; *a*, *b*, *c*, uric acid.



Fig. 331.



Fig. 332.



Fig. 333.



Fig. 334.

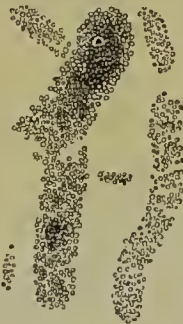


Fig. 335.

Fig. 331.—Epithelial casts. Fig. 332.—Blood cast. Fig. 333.—Leucocyte cast. Fig. 334.—Acid sodic urate in cylinders. Fig. 335.—Finely granular cast.

blue colour (amyloid reaction) with sulphuric acid and iodine. 5. **Blood casts** occur in capillary hæmorrhage of the kidney, and consist of coagulated blood entangling blood-corpuscles (fig. 332). When tube casts are present, the urine is always *albuminous*.

Leucocyte casts occur in suppurating conditions of the urinary tubules (fig. 337). The urates in the form of casts (fig. 334) are without significance.

II. Unorganised Deposits.

Some of these are **crystalline** and others are **amorphous**, and they have been referred to in treating of the urinary constituents.

271. SCHEME FOR DETECTING URINARY DEPOSITS.—I. In acid urine there may occur—

1. An **amorphous granular deposit**:

(*a*) Which is dissolved by heat and reappears in the cold; the deposit is often reddish in colour = **urates** (fig. 316).

- (b) Which is not dissolved by heat but is dissolved by acetic acid, but without effervescence=probably **tribasic calcic phosphate**.
- (c) Small bright refractive granules, soluble in ether=fat or oil granules (§ 41), (Lipæmia). Fat occurs in the urine, especially when the round worm, *Filaria sanguinis hominis*, is present in the blood; sometimes, along with sugar, in phthisis, poisoning with phosphorus, yellow fever, pyæmia, after long-continued suppuration, and lastly, after the injection of fat or milk into the blood (§ 102). It occurs also in fatty degeneration of the urinary apparatus, admixture with pus from old abscesses, and after severe injuries to bones. In these cases attention ought to be directed to the presence of cholesterolin and lecithin. Very rarely is the fat present in such amount in the urine as to form a cream on the surface (chyluria).



Fig. 336.

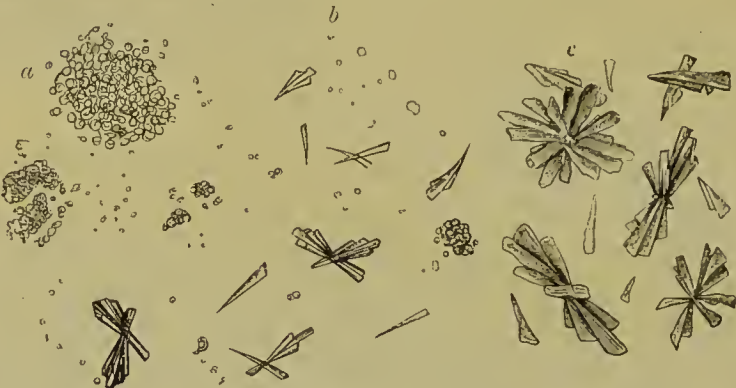


Fig. 338.



Fig. 337.

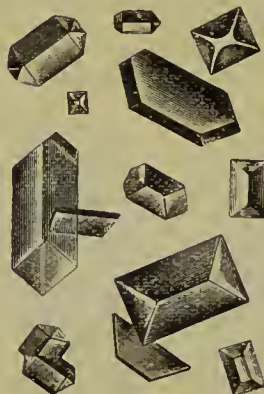


Fig. 339.

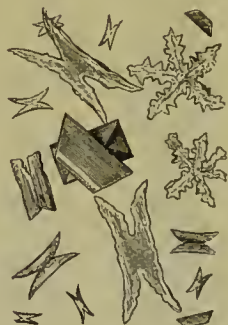


Fig. 340.

Fig. 336.—Coarsely granular casts. Fig. 337.—Hyaline casts, *a*; *b*, with leucocytes; *c*, with renal epithelium. Fig. 338.—*a*, Granules of calcic carbonate of lime; *b*, *c*, crystalline neutral calcic phosphate. Fig. 339.—Ammonio-magnesium phosphate or triple phosphate. Fig. 340.—Imperfect and feathery forms of the same.

2. A crystalline deposit may be—
 - (a) Uric acid (fig. 312).
 - (b) Calcium oxalate (fig. 314)—octahedra insoluble in acetic acid.
 - (c) Cystin (fig. 328).
 - (d) Leucin and tyrosin—very rare (fig. 329).
- II. In alkaline urine there may occur—
 1. A completely amorphous granular deposit, soluble in acids without effervescence = tribasic calcium phosphate.
 2. Sediment crystalline, or with a characteristic form.
 - (a) Triple phosphate (figs. 339, 340), soluble at once in acids.
 - (b) Acid ammonium urate—dark yellowish small balls, often beset with spines, also amorphous (fig. 341).
 - (c) Calcium carbonate—small whitish balls or biscuit-shaped bodies. Acids dissolve them with effervescence (fig. 338).

(d) **Lencin** and **tyrosin** (fig. 329)—very rare.

(e) **Neutral calcic phosphate** and long plates of **tribasic magnesie phosphate** (fig. 342).

Organised deposits may occur both in alkaline and in acid urine; pus-cells are more abundant in alkaline urine, and so are the lower vegetable organisms.

272. URINARY CALCULI.—Urinary concretions may occur in granules the size of sand, or in masses as large as the fist. According to their size they are spoken of as **sand**, **gravel**, **stone**, or **calculi**. They occur in the pelvis of the kidney, ureters, bladder, and sinus prostaticus.

We may classify them as follows (*Ultzmann*):—

1. **Calculi**, whose nucleus consists of the sedimentary deposits that occur in **acid urine** (primary formation of calculi). They are all formed in the kidney, and pass into the bladder, where they enlarge by the deposition of matter on their surface.

2. **Calculi**, which are either sedimentary forms from **alkaline urine**, or whose nucleus consists of a *foreign body* (secondary formation of calculi). They are formed in the bladder.

The **primary** formation of calculi begins with free uric acid in the form of sheaves (fig. 312), which form a nucleus, with concentric layers of oxalate of lime. The **secondary** formation occurs in *neutral* urine by the deposition of calcic carbonate and crystalline calcic phosphate; in *alkaline* urine, by the deposition of acid ammonium urate, triple phosphate, and amorphous calcic phosphate.

Chemical Investigation.—Scrape the calculus, burn the scrapings on platinum foil to ascertain if they are burned or not.

I. Combustible concretions can consist only of organic substances.

(a) Apply the murexide test (§ 259, 2), and, if it succeeds, **uric acid** is present. Uric acid calculi are very common, often of considerable size, smooth, fairly hard, and yellow to reddish-brown in colour.

(b) If another portion, on being boiled with caustic potash, gives the odour of ammonia (or when the vapour makes damp turmeric paper brown, or if a glass rod dipped in HCl and held over it gives white fumes of ammonium chloride), the concretion contains **ammonium urate**. If *b* gives no result, pure uric acid is present. Calculi of ammonium urate are rare, usually small, of an earthy consistence, *i.e.*, soft and pale yellow or whitish in colour.

(c) If the **xanthin** reaction succeeds (§ 260), this substance is present (rare). **Indigo** has been found on one occasion in a calculus (*Ord*).

(d) If, after solution in ammonia, hexagonal plates (figs. 328, A) are found, **cystin** is present.

(e) Concretions of **coagulated blood** or **fibrin**, without any crystals, are rare. When burned they give the odour of singed hair. They are insoluble in water, alcohol, and ether; but are soluble in caustic potash, and are precipitated therefrom by acids.

(f) **Urostealith** is applied to a caoutchouc-like soft elastic substance, and is very rare. When dry it is brittle and hard, brown or black. When warm it softens, and if more heat be applied it melts. It is soluble in ether, and the residue after evaporation becomes violet on being heated. It is soluble in warm caustic potash, with the formation of a soap.

II. If the concretions are only **partly combustible**, thus leaving a residue, they contain organic and inorganic constituents.

(a) Pulverise a part of the stone, boil it in water, and filter while hot. The urates are dissolved. To test if the uric acid is united with soda, potash, lime, or magnesia, the filtrate is evaporated and burned. The ash is investigated with the spectroscope (§ 14), when the characteristic bands of sodium or potash are observed. Magnesic urate and calcic urate are changed into carbonate by burning. To separate them, dissolve the ash in dilute hydrochloric acid, and filter. The filtrate is neutralised with ammonia, and again redissolved by a few drops of acetic acid. The addition of ammonium oxalate precipitates **calcic oxalate**. Filter, and add to the filtrate sodic phosphate and ammonia, when the magnesia is precipitated as **ammonio-magnesic phosphate**.

(b) **Calcic oxalate** (especially in children, either as small smooth pale stones, or in dark, warty, hard "**mulberry calculi**") is not affected by acetic acid, is dissolved by mineral acids without effervescence, and again precipitated by ammonia. Heated on platinum foils it chars and blackens, then it becomes white, owing to the formation of calcic carbonate, which effervesces on the addition of an acid.

(c) **Calcic carbonate** (chiefly in whitish-grey, earthy, chalk-like calculi, somewhat rare,

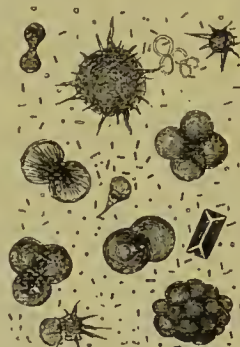


Fig. 341.

Acid ammonium urate.

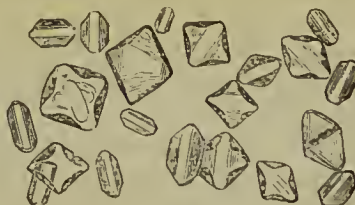


Fig. 342.

Basic magnesic phosphate.

dissolves with effervescence in hydrochloric acid. When burned it first becomes black, owing to admixture with mucus, and then white.

(d) **Ammonio-magnesian phosphate** and **basic calcic phosphate** usually occur together in soft, white, earthy stones, which occasionally are very large. These stones show that the urine has been ammoniacal for a very long time. The first substance when heated gives the odour of ammonia, which is more distinct when heated with caustic potash; is soluble in acetic acid without effervescence, and is again precipitated in a crystalline form from this solution on the addition of ammonia. When heated it fuses into a white enamel-like mass; [hence, it is called "fusible calculus"]. **Basic calcic phosphate** does not effervesce with acids. The solution in hydrochloric acid is precipitated by ammonia. When ammonium oxalate is added to the acetic acid solution, it yields calcic oxalate.

(e) **Neutral calcic phosphate** is rare in calculi, while it is frequent in the form of gravel. Physically and chemically, these concretions resemble the earthy phosphates, only they do not contain magnesia.

273. THE SECRETION OF URINE.—[The functions of the kidney are—

1. To excrete waste products, chiefly nitrogenous bodies and salts;
2. To excrete water;
3. And perhaps also to reabsorb water from the uriniferous tubules, after it has washed out the waste products from the renal epithelium.

The chief parts of the organs concerned in 1, are the epithelial cells of the convoluted tubules; the glomeruli permit water and some solids to pass through them, while the constrictions of the tubules may prevent the too rapid outflow of water, and thus enable part of it to be reabsorbed.]

Theories.—The two chief older theories regarding the secretion of urine are the following: 1. According to **Bowman** (1842), through the glomeruli are filtered only the *water* and some of the highly diffusible and soluble salts present in the blood, while the specific urinary constituents are secreted by the activity of the epithelium of the urinary tubules, and are extracted or removed from the epithelium by the water flowing along the tubules. This has been called the "vital" theory. 2. **C. Ludwig** (1844) assumes that *very dilute urine* is secreted or filtered through the glomerulus. As it passes along the urinary tubules it becomes more concentrated, owing to endosmosis. It gives back some of its water to the blood and lymph of the kidney, thus becoming more concentrated, and assuming its normal character. [This is commonly known as the "mechanical theory."]

The secretion of urine in the kidneys does not solely depend upon definite physical forces. A great number of facts force us to conclude that the vital activity of certain secretory cells plays a foremost part in the process of secretion (*R. Heidenhain*).

The secretion of urine embraces—(1) The **water**, and (2) the **urinary constituents** therein dissolved; both together form the urinary secretion. The **amount of urine** depends chiefly upon the amount of water which is filtered through or secreted by the glomeruli; the **amount of solids** dissolved in the urine determines its **concentration**.

(A) The **amount of urine**, which is secreted chiefly within the Malpighian capsules, *depends primarily upon the blood-pressure in the area of the renal artery*, and follows, therefore, the laws of **filtration** (§ 191, II.) (*Ludwig and Goll*). [In this respect the secretion of urine differs markedly from that of saliva, gastric juice, or bile. We may state it more accurately thus, that the amount of urine depends very closely upon the differences of pressure between the blood in the glomeruli and the pressure within the renal tubules. If the ureter be ligatured, the secretion of urine is ultimately arrested, even although the blood-pressure be high. The secretion may also be arrested by ligature of the renal vein; and in some cases of cardiac pulmonary disease the venous congestion thereby produced may bring about the same result.]

Glomerular Epithelium.—The amount of urine secreted does not depend upon

the hydrostatic pressure alone, but it seems that the epithelial cells covering the glomerulus also participate *actively* in the process of secretion. Besides the water, a certain amount of the salts present in the urine are excreted through the glomeruli. *The serum-albumin of the blood, however, is prevented from passing through.* With regard to the secretory activity of these cells, the quantity of water must also depend upon the amount of the urinary constituents and water present in the blood (*R. Heidenhain*).

Only when the vitality of the secretory cells is intact is there **independent activity** of these secretory cells (*Heidenhain*). When the renal artery is closed temporarily, their activity is paralysed, so that the kidneys cease to secrete, and even after the compression is removed and the circulation re-established, secretion does not take place for some time (*Overbeck*).

That the secretion depends **in part upon the blood-pressure** is proved by the following considerations:—

1. *Increase of the total contents of the vascular system so as to increase the blood-pressure*, increases the amount of water which filters through the glomeruli. The injection of water into the blood-vessels, or drinking copious draughts of water, acts partly in this way. If the blood-pressure rises above a certain height, albumin may pass into the urine. The *active participation* of the cells of the glomeruli is rendered probable by the fact that, after very copious drinking, the blood-pressure is not always raised (*Pawlow*); further, after *copious transfusion*, the quantity of urine is not increased. Conversely, the loss of water owing to profuse sweating or diarrhoea, copious hæmorrhage, or prolonged thirst, diminishes the secretion of urine.

2. *Diminution of the capacity of the vascular system*, provided the pressure within the renal area be thereby increased, acts in a similar manner. This may be produced by contraction of the cutaneous vessels, owing to the action of cold, stimulation of the vaso-motor centre, or large vaso-motor nerves, ligature, or compression of large arteries (§ 85, *e*), or enveloping the extremities in tight bandages. All these conditions cause an increase in the amount of urine, and of course the opposite conditions bring about a diminution of urine, *e.g.*, the action of heat on the skin causing redness and dilatation of the cutaneous vessels, weakening of the vaso-motor centre, or paralysis of a large number of vaso-motor nerves.

3. *Increased action of the heart*, whereby the tension and rapidity of the blood in the arteries are increased (§ 85, *c*), augments the amount of urine; conversely, feeble action of the heart (paralysis of motor cardiac nerves, disease of the cardiac musculature, certain valvular lesions) diminishes the amount. Artificial stimulation of the vagi in animals, so as to slow the action of the heart, and thus diminish the mean blood-pressure from 130 to 100 mm. Hg, causes a diminution in the amount of urine to the extent of one-fifth (*Goll, Cl. Bernard*); when the pressure in the aorta falls to 40 mm. the secretion of urine ceases. [If the medulla oblongata be divided (dog), there is an immediate fall of the *general* blood-pressure, and although, as a general rule, the secretion of urine is arrested when the pressure falls to 40 to 50 mm. Hg, yet secretion has been observed to take place with a lower pressure than this.]

4. The amount of urine secreted *rises or falls according to the degree of fulness of the renal artery* (*Ludwig, Max Hermann*); even when this artery is moderately constricted in animals, there is a decided diminution in the amount of urine.

Pathological.—In fever the renal vessels are less full and there is consecutive diminution of urine (*Mendelsohn*). It is most important, in connection with certain renal diseases, to note that ligature of the renal artery, even when it is obliterated for only two hours, causes necrosis of the epithelium of the uriniferous tubules. When the arterial anæmia is kept up for a long time, the whole renal tissue dies (*Litten*). After long-continued ligation of the renal artery, the epithelium of the glomeruli becomes greatly changed (*Ribbert*).

5. Most diuretics act in one or other of the above-mentioned ways.

[Some diuretics act by increasing the *general* blood-pressure (digitalis and the action of cold on the skin), others may increase the blood-pressure *locally* within the kidney, and this they may do in several ways. The nitrites are said to paralyse the muscular fibres in the vasa afferentia, and thus raise the blood-pressure within the glomeruli. But some also act on the *secretory epithelium*, such as urea and caffeine. Brunton recommends the combination of diuretics in appropriate cases, and the diuretics must be chosen according to the end in view—as we wish to remove excess of fluids from the tissues and serous cavities, or as we wish to remove injurious waste products, or merely to dilute the urine.]

[6. The amount of urine also depends upon the *composition of the blood*. Drinking a large quantity of water, whereby the blood becomes more watery, increases the amount of urine, but this is true only within certain limits. It is not merely the increase of volume of the blood acting mechanically which causes this increase, as we know that large quantities of fluid may be transfused without the general blood-pressure being materially-raised thereby.]

[Heidenhain argues that it is not so much the *pressure* in the glomeruli as the **velocity of the blood**, which determines the process of the secretion of water in the kidney. He contends that, while increase of the pressure in the renal artery causes an increased flow of urine, ligature of the renal vein, whereby the pressure in the glomeruli is also increased, arrests the secretion altogether. In both cases the pressure is increased within the glomeruli, and the two cases differ essentially in the *velocity* of the blood-current through the glomeruli.]

Pressure in the Vas Afferens.—The pressure in each *vas afferens* must be relatively great, because (1) the double set of capillaries in the kidney offers considerable resistance, and (2) the lumen of the vas efferens is narrower than that of the vas afferens. Hence, owing to the high blood-pressure in the capillaries of the renal glomeruli, filtration must take place from the blood into the Malpighian capsules. When the vasa afferentia are dilated, the filtration-pressure is increased, while, when they are contracted, the secretion is lessened. When the pressure becomes so diminished as to retard greatly the blood-stream in the renal vein, the secretion of urine begins to be arrested. **Occlusion of the renal vein** completely suppresses the secretion (*H. Meyer, v. Frerichs*). Ludwig concluded from this observation that the filtration or excretion of fluid could not take place through the renal capillaries *proper*, as, owing to occlusion of the renal vein, the blood-pressure in these capillaries must rise, which ought to lead to increased filtration. Such an experiment points to the conclusion that the *filtration must take place through the capillaries of the glomeruli*. The venous stasis distends the vas efferens, which springs from the centre of the glomerulus, and compresses the capillary loops against the wall of the Malpighian capsule, so that filtration cannot take place through them. It is not decided whether any fluid is given off through the convoluted urinary tubules.

Venous congestion in the kidneys diminishes the quantity of urine and the urea. The NaCl remains constant, but pathological albumin is increased (*Senator and Munk*).

Pressure in Ureter.—As the blood-pressure in the renal artery is about 120 to 140 mm. Hg, and the urine in the ureter is moved along by a very slight propelling force, so that a counter-pressure of from 10 (*Lobell*) to 40 mm. of Hg is sufficient to arrest its flow, it is clear that the blood-pressure can also act as a *vis a tergo* to propel the urine through the ureter. The pressure in the ureter is measured by dividing the ureter transversely and inserting the manometer in it.

(B) Secretory Activity of the Renal Epithelium.—The degree of **concentration** of the urine also depends upon the quantity of the dissolved constituents which has passed from the blood into the urine. The secretory cells of the convoluted tubules, by their own proper vital activity, seem to be able to take up, or secrete, some at least of these substances from the blood (*Bowman, Heidenhain*).

The watery part of the urine, containing only easily diffusible salts, as it flows along the tubules from the glomeruli, extracts or washes out these substances from the secretory epithelium of the convoluted tubules.

Experiments with sulphindigotate of soda.—1. Sulphindigotate of soda and sodium urate, when injected into the blood, pass into the urine, and are found within the protoplasm of the *cells* of the *convoluted tubules* [only in those parts lined by “rodged” epithelium], but not in the Malpighian capsules (*Heidenhain*). A little later these substances are found in the *lumen* of the urinary tubules, from which they are washed out by the watery part of the urine coming from the glomeruli. If, however, two days before the injection of these substances into the blood, the cortical part of the kidney containing the Malpighian capsules be cauterised [*e.g.*, by nitrate of silver], or sliced off, the blue pigment remains within the convoluted tubules. It cannot be carried onward, as the water which should carry it along has ceased to be secreted, owing to the destruction of the glomeruli. This experiment also goes to show that through the *glomeruli* the *watery part* of the urine is *chiefly excreted*, while through the *convoluted tubules* the *specific urinary constituents* are excreted.

[When a large quantity of the pure sulphindigotate is injected into the blood, within less than half an hour the cortex and pyramids become deep blue; the boundary zone, as a rule, is lighter in tint (fig. 343). The blue pigment is found

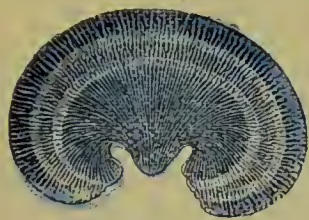


Fig. 343.



Fig. 344.

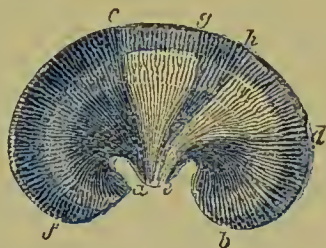


Fig. 345.

Fig. 343.—Section of a rabbit's kidney after the injection of a large quantity of sulphindigotate of soda into the blood. Fig. 344.—Section of a rabbit's kidney. Section of the spinal cord and subsequent injection of sulphindigotate of soda. Note that the pigment is confined to the cortex. Fig. 345.—Section of a rabbit's kidney. The surface between *c* and *g* and *d* and *h* was cauterised. There is the normal appearance in the areas *fc*, *gh*, *db*, but arrest of the secretion of water in *eg* and *hd*.

in the epithelium of the convoluted tubules, or in their lumen, but never in the epithelium of the straight tubules, although a large amount is found in the lumina, especially of the collecting-tubes.]

[If, however, the spinal cord be divided so as to lower the arterial blood-pressure, and thus arrest the secretion of water, and a small quantity of the sulphindigotate be injected into the blood, the blue pigment is secreted from the lymph, itself nearly colourless, by the convoluted tubules and the looped tubules of Henle. Owing to the arrest of the watery part of the secretion, the pigment remains in the cortex and the kidney presents the appearance shown in fig. 344.]

[Fig. 345 shows the effect of canterising the surface of the kidney with silver nitrate. In the cauterised area the secretion of water within the capsules ceases, while the secretion of the pigment by the convoluted tubules is not arrested, so that in the normal areas one has the appearances shown in fig. 343 and in the cauterised area that of fig. 345].

Uric acid salts, injected into the blood, were observed by *Heidenhain* to be excreted by the convoluted tubules. *Von Wittich* had previously observed that in *birds*, crystals of uric acid were excreted by the epithelium of the convoluted tubules. [The presence of crystals of uric acid in the renal epithelium was

observed by Bowman, and used as an argument to support his theory.] Nussbaum, in 1878, stated that *urea* is secreted by the urinary tubules and not by the glomeruli.

The same is true for the *bile-pigments*, for the *iron salts* of the vegetable acids when injected subcutaneously, and for *hæmoglobin*. After injection of *milk* into the blood-vessels, numerous fatty granules occur within the epithelium of the urinary tubules (§ 102).

Excretion of Pigments.—Only during very copious excretion does the glomerulus participate. After the introduction of a large amount of sodic sulphindigotate, and when the experiment has lasted for a long time, the epithelium of the glomerulus becomes blue. In *albuminuria*, the abnormal excretion of urine takes place first in the urinary tubules, and afterwards in the Malpighian capsules; Hb is partly found in the capsules. According to Nussbaum, egg-albumin passes out through the Malpighian capsules.

[Nussbaum's Experiments.—In the *frog* and *newt*, the kidney is supplied with blood in a manner different from that obtaining in mammals. The glomeruli are supplied by branches of the renal artery. The tubules are supplied by the renal-portal vein (fig. 346). The vein coming from the posterior extremities divides at the upper end of the thigh into two branches, one of which enters the kidney, and breaks up to form a capillary plexus, which surrounds the uriniferous tubules, but this plexus is also joined by the efferent vessels of the glomeruli. These two systems are partly independent of each other. After ligaturing the renal arteries, Nussbaum asserted that the circulation in the glomeruli was cut off, while ligature of the renal-portal vein excluded the functional activity of the tubules. By injecting a substance into the blood, after ligaturing either the arteries or renal-portal vein, and observing whether it occurs in the urine, he infers that it is given off either by the glomeruli or the tubules. *Sugar*, *peptones*, and *egg-albumin* rapidly pass through an intact kidney, but if the renal arteries be tied they are not excreted. *Urea* when injected into the circulation is excreted after the arteries are tied, so that it is excreted through the tubules, but at the same time it takes with it a considerable quantity of water. Thus, water is excreted in *two* ways from the kidney, by the glomeruli and also from the venous plexus around the tubules along with the *urea*. *Indigo-carmin* merely passes into the tubular epithelium of the convoluted tubules, but it does not cause a secretion of urine. *Albumin* passes through the glomeruli, but only after their membranes have been altered in some way, as by clamping the renal artery for a time.]

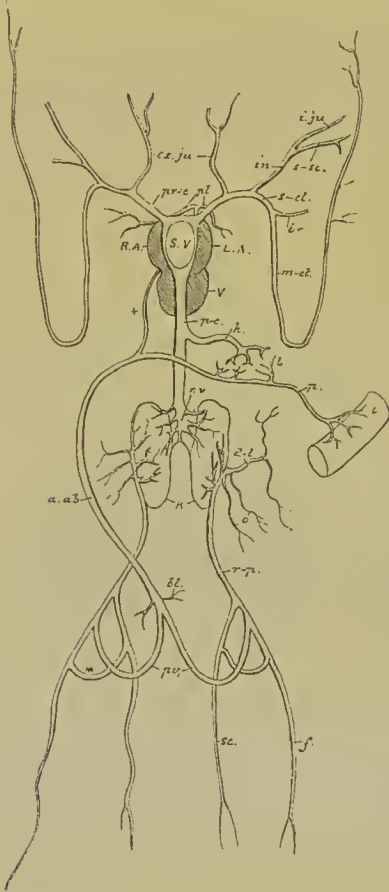


Fig. 346.

Veins of the frog, semi-diagrammatic. *S.V.*, sinus venosus; *RA*, *LA*, right, left auricles; *V*, ventricle; *pr-c*, pre-caval; *ca.ju.*, external jugular; *i.ju.*, internal jugular; *s-sc.*, subscapular; *in.*, innominate; *s-cl.*, subclavian; *br.*, brachial; *m-cl.*, musculo-cutaneous; *pc*, post-caval; *sc*, sciatic; *p.v.*, pelvic; *rp*, renal-portal; *d.-l.* dorso-lumbar; *o*, veins from oviduct; *r.v.*, renal, *a.ab.*, anterior abdominal; *bl.*, vesical; *p*, portal, and *h.*, hepatic veins; *k*, kidneys; *i*, alimentary canal with its capillaries; *l*, capillaries of liver; *pl*, pulmonary veins.

[Adami's Experiments on the kidney of the frog tend to show that Nussbaum's conclusions are not justified, for Adami found that if the renal arteries in the frog be ligatured, within a few hours a collateral circulation is established and a certain amount of blood flows through

the kidney. He proved this by injecting into the blood carmine or painter's vermilion, in a state of fine suspension, and after ligature of the renal arteries he found it in many of the glomeruli, while laky blood similarly injected revealed its presence as menisci of Hb in the Malpighian corpuscles. Even secretion of some urine may go on after ligature of the renal arteries. It is evident, then, that Nussbaum's method is not a reliable one for locating the parts of the kidney through which certain substances are excreted. Adami's experiments also give some support to Heidenhain's view that the glomerular epithelium "possesses powers of a selective secretory nature," for he finds that in frogs, after ligature of the renal arteries, where, of course, the pressure in the glomeruli is just nearly that in the veins, and in the dog after section of the spinal cord, so that the blood-pressure has fallen below 40 mm. Hg, whereby the secretion of urine is arrested, the injection of laky blood causes Hb to appear in the capsules, although there is no simultaneous excretion of water.]

2. Even when the secretion of the *watery part* of the urine is completely *arrested*, either by ligature of the ureter, or after a very great fall of the blood-pressure in the renal artery, [as after section of the cervical spinal cord], the before-mentioned substances, when injected into the blood, are found in the cells of the convoluted tubules. The injection of urea under these circumstances causes renewed secretion. These facts show that, independently of the filtration-pressure, the *secretory activity of these cells* is still maintained.

The independent **vital activity of the secretory cells** of the urinary tubules, which as yet we are unable to explain on purely physical grounds, renders it probable that the tubules are not to be compared to an apparatus provided with physical membranes. This is proved by the following experiment:—Abeles caused arterial blood to circulate through freshly excised living kidneys. A pale urine-like fluid dropped from the ureter. On adding some urea or sugar to the blood, the secretion became more concentrated. Thus, the *excised "surviving" kidney* also excretes substances in a more concentrated form than those supplied to it in the diluted blood streaming through it. J. Munk obtained similar results in excised kidneys, with common salt, nitre, caffeine, grape-sugar, glycerin, with increase in the amount of urine secreted. The addition of caffeine or theobromin to the perfused blood increases the secretion, exciting the secretory cells to greater activity (*v. Schroeder*).

Salts and Gases.—The vital activity explains why the serum-albumin of the blood does not pass into the urine, while egg-albumin and dissolved hæmoglobin readily do so. Among the *salts* which occur in the blood and blood-corpuscles, of course only those in solution can pass into the urine. Those which are united with proteid bodies, or are fixed in the cellular elements, cannot pass out, or at least only after they have been split up. Thus, we may explain the difference between the salts of the urine and those of the blood. Similarly, the urine can only contain the absorbed and not the chemically-united *gases*.

Ligature of the Ureter.—If the secretion be arrested by compression or by ligature of the ureter, the lymph-spaces of the kidney become filled with fluid, which may pass into the blood, so that the organ becomes cedematous, owing to the passage of fluid into its lymph-spaces. The secretion undergoes a change, as first water passes back into the blood, then the sodic chloride, sulphuric, and phosphoric acids diminish, and lastly the urea (*C. Ludwig, Max Herrman*). Kreatinin is still present in considerable amount. There is no longer secretion of proper urine (*Löbell*).

Non-Symmetrical Renal Activity.—It is remarkable that both kidneys do not secrete symmetrically—there is an alternate condition of hyperæmia and secretory activity on opposite sides (§ 100). One kidney secretes a more watery urine, which at the same time contains more NaCl and urea. Von Wittich observed that the secretion of uric acid was not uniform in all the urinary tubules of the same bird. **Extirpation** of one kidney, or disease of one kidney in man, does not seem to diminish the secretion (*Rosenstein*). The remaining kidney becomes more active, and larger.

Reabsorption in the Kidney.—In discussing the secretion of the kidney, we must attach considerable importance to the variations in the calibre of the renal tubules in their course. Perhaps in the narrowing of the descending part of the looped tubule of Henle there may be either a reabsorption of water, so that the urine becomes more concentrated, or there may be absorption even of albumin, which may perhaps pass through the glomeruli in small amount. [That reabsorption of fluid takes place within the kidney was part of Ludwig's theory, which is practically a process of filtration and reabsorption. Hüfner pointed out that the structure of the kidneys of various classes of vertebrates corresponded closely with the requirements for reabsorption of water. The experiments of Ribbert show that the urine actually secreted in the cortex of the kidney is more watery than that secreted normally by the entire organ. He extirpated the medullary portion in rabbits, leaving the cortical part intact, and in this way collected the dilute urine from the Malpighian corpuscles before it passed through Henle's loops.]

274. FORMATION OF THE URINARY CONSTITUENTS.—The question has often been discussed, whether all the urinary constituents are merely excreted through the kidneys, *i.e.*, that they exist preformed in the blood; or whether some of them do *not* exist preformed in the blood, but are formed within the kidneys, as a result of the activity of the renal epithelium.

Urea is formed outside the Kidney.—Urea exists preformed in the blood, from which it is separated by the activity of the kidney. This is proved by the following considerations:—

1. The blood contains one part of urea in 3000 to 5000 parts, but the renal vein contains less urea than the blood of the corresponding artery.

2. After **extirpation** of the kidneys, or **nephrectomy**, or after ligature of the renal vessels, the amount of urea accumulates in the blood, and increases with the duration of the experiment to $\frac{1}{300}$ to $\frac{1}{400}$. At the same time there is vomiting and diarrhoea, and the fluids so voided contain urea (*Cl. Bernard*). Animals die in from one to three days after the operation.

3. After ligature of the ureters, the secretion of urine is soon arrested. Urea accumulates in the blood, but not to a greater extent than after nephrectomy. It is possible, however, that the kidneys, like other organs, may form a small amount of urea, due to the metabolism of their own tissues.

[Although the percentage of urea in the blood is small, yet when we consider the enormous amount of blood circulating through the very vascular kidneys, we obtain data which prove that the kidneys withdraw the urea from the blood. A dog weighing 30 kilos. (66·6 lbs.) has 2·31 kilos. of blood, *i.e.*, $\frac{1}{13}$ th part of its body-weight. The entire course of the circulation is completed in 15 secs., so that in 24 hours $2·31 \times 4 \times 60 \times 24 = 13305·6$ kilos. of blood will pass through the body. Taking the kidneys as $\frac{1}{100}$ part of the weight of the body, about 66·53 kilos. of the blood will pass through the kidneys in 24 hours. Suppose the blood contained only ·5 gram urea in 1000 c.c., 66·53 kilos. could yield 33·3 grams of urea. A large dog fed on flesh excretes 30–35 grams of urea in 24 hours (*Munk*).]

[Urea exists in the blood; whence does the blood derive it? It can only obtain it from one or more of several organs—(1) muscle, (2) nervous system, and (3) glands, of which the liver is the most prominent. This is best stated by the method of exclusion.]

[1. That urea is not formed in muscle is shown, among other considerations, by the fact that only a trace of urea occurs in muscle (§ 293), and that the amount is not increased by exercise. Blood which has been transfused through a muscle, or the blood after circulating in a muscle during violent exercise, does not contain an increase of urea, nor does the addition of ammonium carbonate to blood circulating through muscle show any increase of urea. Again, muscular exertion does not (as a rule) increase the amount of urea in the urine, as shown by the experiments of Fick and Wislicenus (§ 294), Parkes, and others. The excretion chiefly increased by muscular exertion is the pulmonary CO_2 (§ 127).]

[2. From what we know of the nervous system, it is not formed there. We are therefore forced to consider the evidence as to the **liver**, as the organ, or, at least, the chief organ, in which it is formed. This evidence is in some respects contradictory, but it is partly **experimental** and partly **clinical**.]

[**Experimental Evidence.**—Although Hoppe-Seyler denies the existence of urea in the liver, (1) its existence there was proved by Gscheidlen; (2) and Cyon, on passing blood through an excised liver by the “perfusion” method of Ludwig, found that blood, after being passed several times through the organ, contained an *increased* amount of urea. The objection to these experiments is that Cyon’s method of estimating the urea was unreliable. (3) But von Schroeder, using a similar method, finds that if blood taken from a dog in *full digestion* be perfused through the liver, there is a slight increase in the amount of urea, while there is no urea formed when the blood of a fasting dog is similarly perfused. (4) If ammonium carbonate be added to the blood, there is a very much greater amount of urea in the blood of the hepatic vein. This last fact is confirmed by Salomon. But if blood mixed with ammonium carbonate be perfused through an excised surviving kidney, or through the muscles of the lower limbs, there is no increase

of urea. These experiments seem to point to ammonium carbonate as being one of the antecedents of urea, which is further strengthened by the fact that the administration of ammonium salts increases the amount of urea in the urine. (5) The experiments of Minkowski on the liver of the goose (§ 386) show that, when the liver is excluded from the circulation, lactic acid takes the place of uric acid in this bird. (6) Brouardel further states, that if the region of the liver be so beaten as to cause congestion of that organ, there is an increase of the urea in the urine. (7) Noël-Paton finds that some drugs which increase the quantity of bile in dogs in a state of N-equilibrium (§ 178), *e.g.*, sodic salicylate and benzoate, colicium, mercuric chloride, and euonymin, also increase the urea in the urine; he therefore concludes "that the formation of urea in the liver bears a very direct relationship to the secretion of bile by that organ." But the destruction of red blood-corpuscles, *e.g.*, by the injection of pyrogallie acid or toluylendiamin into the blood by setting free hæmoglobin, not only causes an increase of bile, but it also increases the elimination of urea by the kidneys, and the time of maximum destruction of the red blood-corpuscles, as measured by the hæmocytometer, coincides with the maximum excretion of urea.]

[The **clinical evidence** points strongly to the formation of urea in the **liver**. Parkes pointed out that in hepatic abscess, during the early congestive stage, the urea in the urine is increased, while it is diminished in the suppurative stage, when the hepatic parenchyma is destroyed. The urea is also diminished in cancer of the liver, phthisis, and some forms of hepatic cirrhosis, while it is increased during hepatic congestion, and specially so in some cases of diabetes mellitus. The most striking fact of all is that, in **acute yellow atrophy** of the liver, the urea is enormously diminished in the urine, and may even disappear from it while its place is taken by the intermediate products, leucin and tyrosin (*v. Frerichs*). In poisoning by phosphorus, coincident with the atrophy of the liver, there is a fall in the urea-excretion. In diabetes mellitus depending on disease of the liver, not only is the sugar passed in the urine greatly increased, but the urea is also increased. In hepatic cirrhosis, where there is great diminution in the parenchyma of the liver, the urea in the urine is greatly diminished and the ammonia greatly increased.]

As to the **antecedents** of urea there is the greatest doubt (§ 256).

[These and the following experiments indicate that urea, and perhaps most of the organic urinary constituents, are "secreted" or separated by the kidneys from the blood passing through them, and that they are not formed in the kidneys themselves. The **urea** is derived from proteids, and the **liver** seems to be the organ in which it is formed.

Uric Acid is formed outside the Kidneys.—1. Bird's blood normally contains uric acid (*Meissner*). [The liver of the pigeon contains 6 to 14 times as much uric acid as the blood.] Ligature of the ureters or renal blood-vessels (*Pawlinoff*), or gradual destruction of the renal secretory parenchyma by the subcutaneous injection of neutral potassium chromate (*Ebstein*), is followed by the deposition of uric acid in the joints and tissues, and it may even form a white incrustation on the serous membranes. The brain remains free (*Zalesky, Oppler*). Acid urates of ammonia, soda, and magnesia are also similarly deposited. Extirpation of a snake's kidneys gives the same result, but to a less degree.

[Minkowski found that, after excluding the liver from the circulation, lactic acid took the place of uric acid in the urine (p. 498). Some uric acid still appears in the urine, which cannot be derived from the small amount in the blood, so that, according to *v. Schroeder*, there are perhaps other foci of formation of uric acid.]

[The latter experiment points to the formation of **uric acid** in the liver in birds, and this is supposed to be strengthened by the appearance of the deposition of urates in the urine in certain disorders of digestion.] Von *Schroeder* and *Colasanti*,

however, as the result of their experiments upon snakes, come to the conclusion that there is no special organ concerned in the formation of uric acid.

Hippuric acid is partly formed in the kidney, for the blood of herbivora does not contain a trace of it (*Meissner and Shepard*). In rabbits, however, it is formed synthetically in other tissues as well as in the kidney. If blood containing sodic benzoate and glycine be passed through the blood-vessels of a fresh kidney, hippuric acid is formed (§ 260) (*Bunge, Schmiedeleberg, Kochs*). [The other evidence is given in § 260.]

Kreatinin has intimate relations to kreatin of muscle, but where it is formed is not known.

If *phenol* and *pyrokatechin* are digested along with fresh renal substance, a compound of sulphuric acid similar to that occurring in urine is formed (§ 262). The latter substance, however, is also formed by similarly digesting liver, pancreas, and muscle. It is concluded from these experiments that these substances are formed in the body within the kidneys and the other organs mentioned (*Kochs*).

[**Urobilin**, nearly related to bilirubin, is ultimately formed from hæmoglobin (§ 261), perhaps in the liver, and is re-absorbed from the intestinal canal to be excreted in the urine. The other urinary pigments all arise directly or indirectly from hæmoglobin, some of them perhaps from the bile pigments, and it may be that they assume their final form in the epithelium of the renal tubules.]

Chemistry of the Kidney.—The kidneys contain a very large amount of water. Besides serum-albumin, globulin, albumin soluble in sodium carbonate (*Gottwalt*), gelatin-yielding substances, fat in the epithelium, elastic substance derived from the membrana propria of the tubules, the kidneys contain leucine, xanthine, hypoxanthine, kreatin, taurine, inosine, cystine (the last in no other tissue), but only in very small amount. The occurrence of these substances points to a lively metabolism in the kidneys, which is also proved by the liberal supply of blood they receive.

Blood-vessels of the Kidney.—The kidneys receive a very large supply of blood, and during secretion the blood of the renal vein is bright red. [In the dog the diameter of the renal artery may be diminished to .5 mm. without the amount of blood flowing through the kidney being thereby greatly interfered with. Hence, within wide limits, the amount of blood is independent of the size of the arterial lumen, and is therefore dependent on the blood-pressure in the aorta, and the resistance to the blood-current within and beyond the kidney (*Heidenhain*).]

The reaction of the kidneys is acid, even in those animals whose urine is alkaline. Perhaps this fact is connected with the retention of the albumin in the vessels.

275. PASSAGE OF VARIOUS SUBSTANCES INTO THE URINE.—1. The following substances pass unchanged into the urine:—Sulphate, borate, silicate, nitrate, and carbonate of the alkalis; alkaline chlorides, bromides, iodides; potassium sulphocyanide and ferrocyanide; bile salts, urea, kreatinin; cumarine, oxalic, camphoric, pyrogallie, and carboic acids. Many alkaloids, e.g., morphia, strychnia, curare, quinine, caffeine; pigments, sulphindigotate of soda, carmine, madder, logwood, colouring matter of cranberries, cherries, rhubarb; santonin; lastly, salts of gold, silver, mercury, antimony, arsenic, bismuth, iron (but not lead), although the greatest part of these is excreted by the bile and the feces.

2. Inorganic acids reappear in man and carnivora as neutral salts of ammonia; in herbivora, as neutral salts of the alkalis.

3. Certain substances which, when injected in small amount, seem to be decomposed in the blood, pass in part into the urine, when they occur in such large amount in the blood that they cannot be completely decomposed—sugar, hæmoglobin, egg-albumin, alkaline salts of the vegetable acids, alcohol, chloroform.

4. Many substances appear in an oxidised form in the urine—moderate quantities of organic alkaline salts, as alkaline carbonates (*Wöhler*), uric acid in part as allantoin (*Salkowski*), sulphides and sulphites of soda, in part as sodium sulphate, potassium sulphide as potassium sulphate, some oxyduls as oxides, benzol as phenol (*Naunyn and Schulzen*).

5. Those bodies which are completely decomposed, as glycerin, resins, give rise to no special derivatives in the urine.

6. Many substances combine and appear as conjugated compounds in the urine, e.g., the origin of the hippuric acid by conjugation (§ 260), the conjugation of sulphuric acid (§ 262), and the formation of urea by synthesis from carbamic acid and ammonia (*Drechsel*) (§ 256). After the use of camphor, chloral, or butylchloral, a conjugated compound with glycuronic acid (an acid nearly related to sugar) appears in the urine (p. 517). [Chloral appears as urochloralic acid, and chloroform partly as urochloralic acid; gallic and pyrogallie acids partly as such,

and partly as pyrogallol, pyrokatechin, and other substances which turn brown when alkaline urine is exposed to the air.] Taurin and sarcosin unite with sulphaminic acid. When bromophenol is given, it unites with mercapturic acid, a body nearly related to cystin (§ 268).

7. Tannic acid, $C_{14}H_{10}O_9$, takes up H_2O , and is decomposed into two molecules of gallic acid = $2(C_7H_6O_5)$.

8. The iodates of potash and soda are reduced to iodides; malic acid ($C_4H_6O_5$) partly to succinic acid ($C_4H_6O_4$); indigo-blue ($C_{16}H_{10}N_2O_2$) takes up hydrogen and becomes indigo-white ($C_{16}H_{12}N_2O_2$).

9. Some substances do not pass into the urine at all, *e.g.*, oils, insoluble metallic salts and metals.

276. INFLUENCE OF NERVES AND OTHER CONDITIONS.—At present we are acquainted merely with the influence of the **vaso-motor nerves** on the circulation through the renal vessels. *Each* kidney seems to be supplied with vaso-motor nerves, which spring from *both* halves of the spinal cord (*Nicolaides*). As a general rule, dilatation of the branches of the renal artery, chiefly the vasa afferentia, must raise the pressure within the glomeruli, and thus increase the amount of water filtered through them. The more the dilatation is confined to the area of the renal artery alone, the greater is the amount of the urine. In the dog, the lower dorsal nerves contain the most vaso-motor nerves—both vaso-constrictor and vaso-dilator (p. 534)—for the kidney (*Bradford*). [As yet we know the nervous system influences the secretion of urine only in so far as it modifies the pressure and velocity of the blood-current in the kidney. We have no satisfactory evidence of the existence of direct secretory nerves in the kidney.]

1. **Renal Plexus and its Centre.**—Section of the nerves of the renal plexus—the nerves around the renal artery—generally causes a considerable increase in the secretion of urine, **hydruria** or **polyuria**; sometimes, on account of the great rise of the pressure within the glomeruli, albumin passes into the urine, and there may be rupture of the vessels of the glomeruli, leading to the passage of blood into the urine. The **nerve-centre** for the renal nerves lies in the floor of the fourth ventricle, in front of the origin of the vagus. Injury to this part of the floor of the fourth ventricle, *e.g.*, by puncture (piqûre), may increase the amount of urine (**diabetes insipidus**), which is sometimes accompanied by the simultaneous appearance of albumin and blood in the urine (*Cl. Bernard*). Section of the parts which lie directly in the course of these fibres, as they pass from their centre to the kidney, produces the same effects. Close to this centre in the medulla lies the centre for the vaso-motor nerves of the liver, whose injury causes **diabetes mellitus** (§ 175). Eckhard found that stimulation of the vermiform process of the cerebellum produced hydruria. In man, stimulation of these parts by tumours or inflammation, &c., produces similar results.

2. **Paralysis of Limited Vascular Areas.**—If, simultaneously with the paralysis of the nerves of the renal artery, the nerves of a neighbouring large vascular area be paralysed, necessarily the blood-pressure in the renal artery area will not be so high, as more blood flows into the other paralysed province. Under these circumstances, there may be only a temporary, or, indeed, no increase of urine, provided the paralysed area be sufficiently large. There is a moderate increase of urine for several hours after **section of the splanchnic nerve**. This nerve contains the renal vaso-motor nerves (which, in part at least, leave the spinal cord at the first dorsal nerve and pass into the sympathetic nerve), but it also contains the vaso-motor nerves for the large area of the intestinal and abdominal viscera. Stimulation of this nerve has the opposite effect (*Cl. Bernard, Eckhard*). [The polyuria thus produced is not so great as after section of the renal nerves, because the splanchnic supplies such a large vascular area, that much blood accumulates in that area, and also because all the renal nerves do not run in the splanchnics.]

3. **Paralysis of Large Areas.**—If, simultaneously with paralysis of the renal nerves, the great majority of the vaso-motor nerves of the body be paralysed [as by

section of the medulla oblongata], then, owing to the great dilatation of all these vessels, the blood-pressure falls at once throughout the arterial system. The result of this may be, provided the pressure is sufficiently low, that there is a great decrease or, it may be, entire cessation of the secretion of urine. The secretion is arrested when the cervical cord is completely divided, down even as far as the seventh cervical vertebra (*Eckhard*). The polyuria caused by injury to the floor of the fourth ventricle at once disappears when the spinal cord (even down to the twelfth dorsal nerve) is divided.

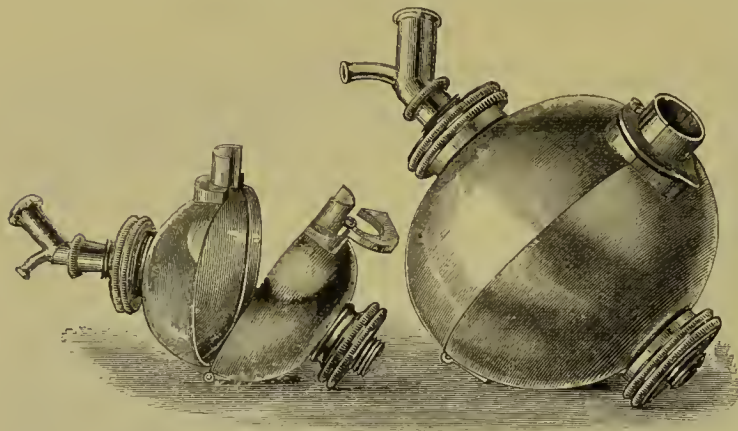


Fig. 347.

View of renal oncometer; the small one is shown open.

throughout the body still further raises the blood-pressure within the glomeruli. If, however, the spinal cord be divided below the medulla oblongata—the renal nerve being also divided—the polyuria ceases, because of the fall of the general blood-pressure thereby produced. Division of the spinal cord in the dorsal region

[4. Other Conditions.

—As already stated, section of the renal nerves is followed by polyuria, owing to the increased pressure in the glomeruli, but this polyuria may be increased by stimulating the spinal cord below the medulla oblongata, because the contraction of the blood-vessels

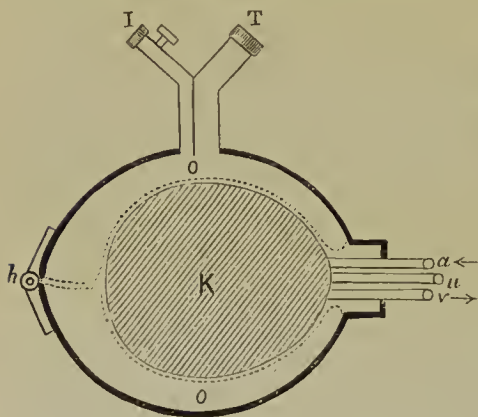


Fig. 348.

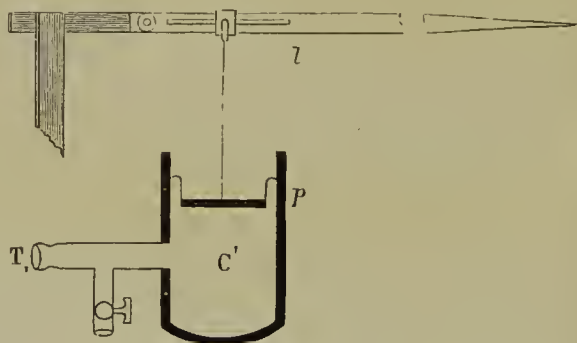


Fig. 349.

Fig. 348.—Oncometer. K, kidney; the thick line is the metallic capsule; h, hinge; I, tube for filling apparatus; T, tube to connect with T_1 ; a, v, u, artery, vein, ureter (*Stirling, after Roy*). Fig. 349.—Oncograph. C', chamber filled with oil, communicating by T_1 with T; p, piston; l, writing-lever (*Stirling, after Roy*).

also diminishes or arrests the secretion of urine, owing to the fall of the blood-pressure; but animals recover from this operation, the general blood-pressure rises, and with it the secretion of urine. Stimulation of the cord below the medulla arrests the secretion, as it causes contraction of the renal arteries along with the other arteries of the body.]

[Volume of the Kidney—Oncometer.—By means of the plethysmograph (§ 101)

we can measure the variations in the size of a limb, while by the oncograph (*ὄγκος*, volume) similar variations in the volume of the spleen are measured (§ 103). Roy and Colnheim have measured the variations in the volume of the kidney by means of an instrument which consists of two parts, one termed the **oncometer** or **renal plethysmometer**, in which the organ is enclosed, while the other part is the registering portion or **oncograph**. The kidney is enclosed in a kidney-shaped metallic capsule (figs. 347, 348), composed of two halves which move on the hinge, *h*, to introduce the organ. The renal vessels pass out at *a*, *v*. The kidney is surrounded with a thin membrane, and between this membrane and the inner surface of the capsule is a space filled with warm *oil* through the tube, *I*, which is closed by means of a stop-cock after the space is filled with oil. The tube *T* can be made to communicate with another tube, *T*₁, leading into a metallic chamber, *C*, of the oncograph (fig. 349), which is provided with a movable piston, *p*, attached by a thread to the writing-lever, *l*. Any increase in the size of the organ expels oil from the chamber, *O*, into *C*, and thus the piston is raised, while a diminution in the size of the kidney diminishes the fluid in *C*, and the lever falls. The actual volume of the living kidney depends upon the state of distention of its structural elements, upon the amount of lymph in its lymph-spaces, but chiefly upon the amount of blood in its blood-vessels, and this again must depend upon the condition of the non-striped muscles in the renal arteries. When the vessels dilate, the kidney increases in size, and when they contract it contracts, so that we can register on the same revolving cylinder the variations of the volume at the same time that we record the general arterial blood-pressure.]

[In the **normal circulation** through the kidney, the kidney-curve, *i.e.*, the curve of the volume of the kidney, runs parallel with the blood-pressure curve, and shows

B. P.

K.

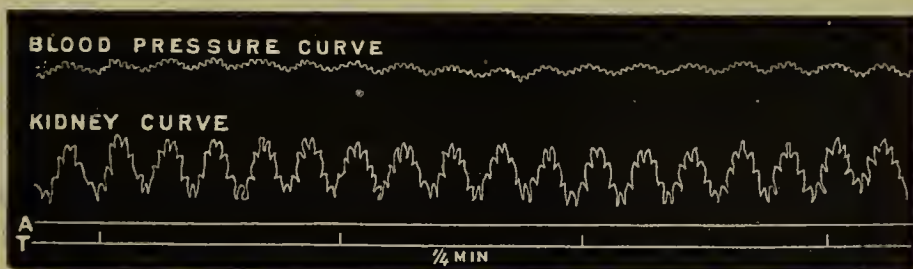


Fig. 350.

B. P., Blood-pressure curve ; K., curve of the volume of the kidney ; T, time curve : intervals indicate a quarter of a minute ; A, abscissa (*Stirling, after Roy*).

the large respiratory undulations, as well as the smaller elevations due to the systole of the heart (fig. 350). In this respect it differs sharply from a spleen-curve (fig. 140). Usually, when the blood-pressure falls, the kidney-curve sinks, and when the blood-pressure rises the volume of the kidney increases. When the blood-pressure curve is complicated by Traube-Hering waves (§ 85) the *opposite* effect is produced on the kidney-curve ; the highest blood-pressure corresponds to the smallest size of the kidney, and conversely. This is due to the fact that, when these curves occur, all the small arterioles, including those in the kidney, are contracted. A kidney placed in an oncometer secretes urine like a kidney under natural conditions.]

[**Arrest of the respiration** in a curarised animal produces a rapid and great diminution of the volume of the kidney, caused by the venous blood stimulating the vaso-motor centres, and thus contracting the small arterioles, including those of the kidney. This result occurs whether one or both splanchnics are divided, proving that all the vaso-motor nerves of the kidney do not reach it through the splanchnics. When *all* the renal nerves at the hilum are divided, arrest of the respiration

causes dilatation of the organ, which condition runs parallel with the rise of the blood-pressure. Stimulation of a sensory nerve, *e.g.*, the central end of the sciatic nerve, while causing an increase of the blood-pressure, makes the kidney shrink.]

[In poisoning with **strychnin**, the kidney shrinks while the blood-pressure rises. Stimulation of the central or peripheral end of the **splanchnics**, divided at the diaphragm, causes contraction of the renal vessels of *both* sides; the former is a reflex, the latter a direct effect. Stimulation of the peripheral end of *one* splanchnic sometimes affects both kidneys. Stimulation of the peripheral end of the renal nerves always causes a diminution in the volume of the kidney, so that Cohnheim and Roy inferred that, although there was evidence of the existence of **vaso-motor** and **sensory nerves** to the kidney, they found none of vaso-dilators. Each kidney acts independently of the other. Sudden compression of one renal artery has not the slightest effect upon the blood-current of the other kidney. If a kidney be exposed in an animal, by making an incision in the lumbar region, on stimulating the medulla oblongata directly with electricity, we may observe the kidney itself becoming paler, the pallor appearing in a great many small spots on the surface of the organ, corresponding to the distribution of the interlobular arteries.]

[Cohnheim showed that the **chemical composition of the blood** has a remarkable effect on the renal circulation, the kidney being very sensitive to such changes in the composition of the blood. Some substances (water and urea), when injected into the blood, cause the kidney first to shrink and then to expand, while sodic acetate dilates the kidney, even after all the renal nerves are divided—an operation which is very difficult indeed. Provided all the renal nerves be divided, these effects would indicate the existence of some local intra-renal vaso-motor mechanism governing the renal blood-vessels. The general blood-pressure is not thereby modified; nor need we wonder at this, as ligature of one renal artery does not increase the pressure in the aorta.]

[**Vaso-constrictor and vaso-dilator nerves to kidney.**—Rose and Bradford, by enclosing the kidney of a dog in an oncometer-tube confirmed the view, that not only are the kidneys well supplied with vaso-constrictor fibres, but that they also receive vaso-dilator fibres. The **vaso-constrictor fibres** leave the spinal cord (dog) by the anterior roots of the spinal nerves as high as the 6th dorsal, and as low as the 2nd lumbar, (or even 4th); but by stimulating the peripheral end of each nerve-root singly, and observing the effect on the volume of the kidney, it has been shown that the largest number pass out by the 11th, 12th, and 13th dorsal nerves. From the anterior roots they enter the corresponding ganglia of the sympathetic, they enter the solar plexus, and pass *viâ* the renal plexus into the kidney. Some apparently do not enter the splanchnic nerve. Vaso-constrictor nerves are best excited by rapid electrical stimulation.]

[**Vaso-dilator fibres.**—It is a peculiarity of vaso-dilator fibres that they are best excited by *slow* rhythmical stimulation (§ 372) (2–5 shocks per sec.), and if the peripheral end of the anterior roots of certain of these nerves be stimulated the kidney dilates, showing that these nerves contain vaso-dilator as well as vaso-constrictor fibres and the vaso-dilators seems to take the same course as the constrictors, being most abundant in the 11th, 12th, and 13th dorsal nerves.]

[The reciprocal relation between the **skin and the kidneys** is known to every one. On a cold day, when the skin is pallid, owing to contraction of the cutaneous vessels, the amount of urine secreted is great, and conversely, in summer less urine is passed than in winter. Washing the skin of a dog for two minutes with ice-cold water causes a great contraction of the kidney.]

The **perfusion of blood through a living excised kidney**, *i.e.*, a “**surviving kidney**,” is materially influenced by the substances mixed with the blood perfused. This effect may in part be due to the action of these chemical ingredients upon the

nuclei of the endothelial lining of the blood-vessels, especially the capillaries, or the effects upon the muscular fibres of the blood-vessels.

[Strychnin seems to cause contraction of the renal vessels, independently of its action on the general vaso-motor centre. Brunton and Power found that digitalis caused an increase of the blood-pressure (dog), but the secretion of urine was either at the same time diminished, or it ceased altogether. The latter result was due to contraction of the renal blood-vessels, but when the aortic blood-pressure began to fall, the amount of urine secreted rose much above normal *i. e.*, when the arteries had begun to relax.]

During fever, the renal vessels are probably contracted in consequence of the stimulation of the renal centre by the abnormally warm blood (*Mendelsohn*).

The repeated respiration of CO is said to produce polyuria, perhaps in consequence of paralysis of the renal vaso-motor centre.

Action of the Vagus.—According to Cl. Bernard, stimulation of the vagus at the cardia increases the urinary secretion, while at the same time the blood of the renal vein becomes red. This nerve may contain vaso-dilator nerve-fibres corresponding to the fibres in the facial nerve for the salivary glands (§ 145).

According to Arthaud and Butte, stimulation of the peripheral end of the vagus diminishes the blood-stream in the kidney and the secretion of urine. Atropin, however, prevents this from taking place. The vagus, therefore, would appear to contain some vaso-motor fibres for the kidney. Stimulation of the cervical sympathetic also diminishes the secretion. This seems to be due to a reflex effect through the spinal cord affecting the splanchnics (*Masius*).

277. URÆMIA—AMMONIÆMIA.—Symptoms of Uræmia.—After excision of the kidneys, nephrectomy, or ligature of the ureter; in man also, as a result of certain diseased conditions of the kidney, leading to the suppression of the secretion of urine, there is developed a series of characteristic symptoms which are followed by death. The condition is called uræmic intoxication, or *uræmia*. There are marked cerebral phenomena, drowsiness, and deep coma, and occasionally local or more general *spasms*. Sometimes there is *delirium*; Cheyne-Stokes' phenomenon is often observed (§ 111, II.), and there may be vomiting and diarrhœa, while in the fluids voided, as well as in the expired air, ammonia may sometimes be detected.

The cause of these phenomena has been ascribed to the retention in the blood of those substances which normally are excreted by the urine, but as yet it has not been definitely ascertained which of these substances causes the phenomena:—

1. The first thought is to ascribe them to the retention of the urea. V. Voit found that dogs exhibited uræmic symptoms if they were fed for a long time on food containing urea and little water. Meissner found that in nephrectomised animals the uræmic symptoms were hastened by the injection of urea into the blood. The injection of a moderate amount of urea in perfectly healthy animals is not followed by uræmic symptoms, probably because the urea is rapidly excreted by the kidneys; 1 to 2 grams [15 to 30 grains] so injected produce comatose symptoms in rabbits. Dogs died in convulsions after the subcutaneous injection of urea equal to 1 per cent. of their body-weight. Although animals die with convulsions after the injection of urea, this is not to be confounded with the intermittent convulsions of uræmic poisoning.

2. The injection of ammonium carbonate produces symptoms resembling those of uræmia, so that v. Frerichs thought that the urea was decomposed in the blood, yielding ammonium carbonate—*ammoniæmia*. Demjankow observed uræmic phenomena after nephrectomy, if at the time he injected urea-ferment into the blood (§ 263). Neither after nephrectomy alone, nor with simultaneous injection of urea into the blood, has any ammonia been found in the blood. It seems, therefore, that the spontaneous formation of urea cannot take place in the blood, and it cannot be the cause of uræmic convulsions. Feltz and Ritter obtained uræmic symptoms in dogs by injecting salts of ammonia into the blood.

3. As ligature of the ureters produces a comatose condition in those animals which excrete chiefly *uric acid* in the urine—*e.g.*, birds and snakes (*Zalesky*)—it is possible that other substances may produce the poisonous symptoms. The injection of *kreatinin* causes feebleness and contraction of the muscles in dogs (*Meissner*). Bernard, Traube, and more recently Feltz and Ritter, ascribe the symptoms to an accumulation of the neutral potassium salts in the blood (§ 54). The injection of kreatin, succinic acid (*Meissner*), uric acid, and sodic urate (*Ranke*), is without effect. Schottin and Oppler ascribe the results to an accumulation of normal or abnormal *extractives*. It is possible that several substances and their decomposition-products contribute to produce the result, so that there is a combined action of several factors, but perhaps the retention of the *potash salts* plays the most important part.

The direct application of some urinary substances (*kreatinin*, kreatin, acid potassic phosphate, urates) to the surface of the cerebrum causes all the symptoms of uræmia. Urea is inactive, and slightly active are ammonium and sodic carbonate, leucin, NaCl, KCl (*Landois*).

[Alkaloids in Urine.]—Human urine, and especially febrile urine, when injected under the skin of frogs or rabbits, acts as a poison, and even causes death, by arresting the respiration.

The alkaloids, *i.e.*, ptomaines and leucomaines, seem to be formed by the action of vegetable organisms in the intestine, whence they are absorbed into the blood, and pass into the urine (§ 116). This, however, is denied by some observers, who state that normal urine is free from such bodies. Urine rendered colourless by chloroal loses half its toxic power, and the poisonous substance is not volatile, and even resists boiling. These alkaloids are increased in the urine in typhoid fever, pneumonia, but not in diabetes.]

Uric Acid Diathesis.—When too much nitrogenous food, too much of any alcoholic fluid is persistently used, and little muscular exercise taken, especially if the respiratory organs are interfered with, uric acid may not unfrequently accumulate in the blood (*Garrod*). It may be deposited in the joints and their ligaments, especially in the foot and hand, giving rise to painful inflammation, and forming gout-stones or chalk-stones [which are acid-nrates]. The heart, liver, and kidneys are rarely affected. The tissues near these deposits undergo necrosis.

278. STRUCTURE AND FUNCTIONS OF THE URETER.—Mucous



Fig. 351.

Transverse section of the lower part of human ureter, $\times 15$. *e*, epithelium; *t*, tunica propria; *s*, sub-mucosa; *l* and *r*, longitudinal and circular fibres.

Membrane.—The pelvis of the kidney and the ureter are lined by a **mucous membrane**, consisting of connective-tissue, and covered with several layers of stratified “**transitional**” epithelium (fig. 352). The cells are of various shapes, those of the lowest layer being usually more or less spherical and small, while many of the cells in the upper layers are irregular in shape, often with long processes passing into the deeper layers.

Sub-mucosa.—Under the epithelium there is a layer of adenoid tissue (*Hamburger, Chiari*), which may contain small lymph-follicles [embedded in loose connective-tissue]. In the pelvis of the kidney and ureter there are a few small mucous glands lined

by a single layer of columnar epithelium (*Umrath, Egli*).

The **muscular coat** consists of an inner somewhat stronger layer of *longitudinal* non-striped fibres, and an outer *circular* layer (fig. 351). In the lowest third of the ureter there are in addition a number of scattered muscular fibres. All these layers are surrounded and supported by connective-tissue. The outer layers of the connective-tissue form an outer coat or **adventitia**,

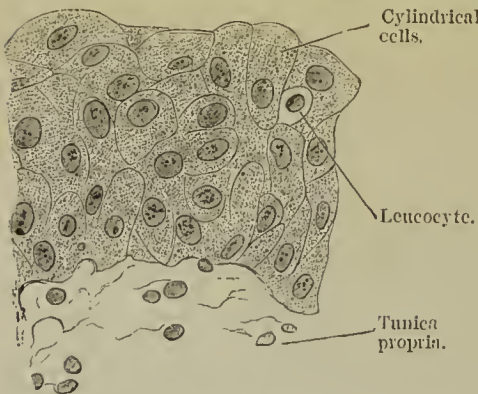


Fig. 352.

Vertical section of the mucous membrane of a human bladder.

which contains the large vessels and nerves. The various coats of the ureter can be followed up to the pelvis of the kidney, and to its calices. The papillae are covered only by the mucous membrane, while the muscular layer ceases at the apex of the pyramids, where they are disposed circularly, to form a kind of *sphincter* muscle for each papilla (*Hentle*).

The **blood-vessels** supply the various coats, and form a capillary plexus under the epithelium. The **nerves** are not very numerous, but they contain medullated (few) and non-medullated fibres, with numerous ganglia scattered in their course. They are partly *motor* and supply the

muscular layers, and some pass towards the epithelium, and are *sensory* and *excito-reflex* in function. These nerves are excited when a calculus passes along the ureter, and thus give rise to severe pain. The ureter perforates the wall of the bladder *obliquely*. The inner opening is a narrow slit in the mucous membrane, directed downwards and inwards, and provided with a pointed valve-like process (fig. 354).

Movement of the Urine.—The urine is propelled along the ureter thus:—(1) The secretion, which is continually being formed under a high pressure in the kidney, propels the urine onwards in front of it, as the urine is under a low pressure in the ureter. (2) *Gravity* aids the passage of the urine when the person is in the erect posture. (3) The muscles of the ureter contract rhythmically and peristaltically, and so propel it towards the bladder. This movement is reflex, and is due to the presence of the urine in the ureter. Every three-quarters of a minute several drops of urine pass into the bladder. But the fibres may also be excited directly. The contraction passes along the tube at the rate of twenty to thirty mm. per second, always from above downwards. The greater the tension of the ureter due to the urine, the more rapid is the peristaltic movement.

Local Stimulation.—On applying a stimulus to the ureter directly, the contraction passes both upwards and downwards.

Engelmann observed that the movements occur in parts of the ureter where neither nerves nor ganglia were to be found, and he concluded that the movement was propagated by “**muscular conduction**.” If this be so, then an impulse may be propagated from one non-stripped muscular cell to another without the intervention of nerves (see Heart, § 58, I., 3).

Prevention of Reflux.

—The urine is prevented from exerting a backward pressure towards the kidneys:—(1) The urine which collects in the pelvis of the kidney is under a high pressure, and thus tends uniformly to compress the pyramids so that the urine cannot pass into the minute orifices of the urinary tubules. (2) When there is a considerable accumulation of urine in a ureter, *e.g.*, from the presence of an impacted calculus or other cause, there is also more energetic peristalsis, and, at the same time, the circular muscular fibres round the apices of pyramids compress the pyramids and prevent the reflux of urine through the collecting tubules. The urine is prevented from passing back from the bladder into the ureter, the wall of the bladder itself, and the part of the ureter which passes through it, are compressed, so that the



Fig. 353.

Isolated transitional epithelium from the bladder of a guinea-pig. Some of the large cells lie upon the summit of the columnar and caudate cells, and depressions are seen on their under surface. *a*, a superficial cell seen from the side, and *a'* from below; *b*, and *c*, cells from the deeper layers. $\times 300$ (*Stirling*).

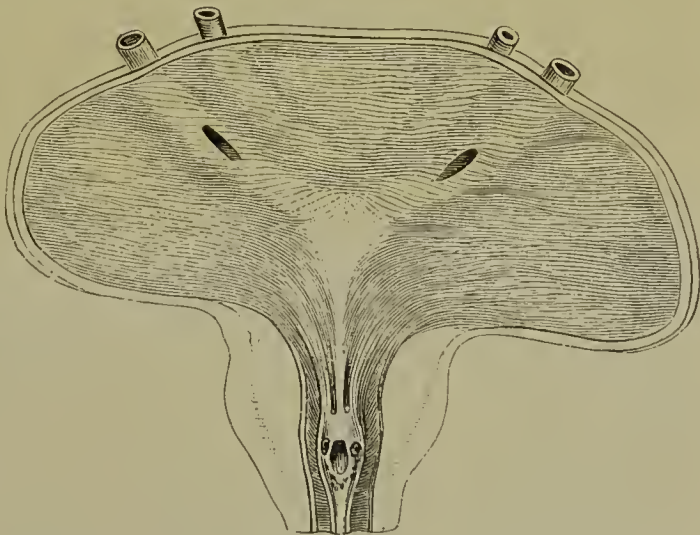


Fig. 354.

Lower part of the human bladder laid open, showing clear part, or trigone, the slit-like openings of the ureters, the divided ureters, and vesiculæ seminales; the sinus prostaticus, and on each side of it the openings of the ejaculatory ducts, and below both numerous small apertures of the prostatic ducts.

edges of the slit-like opening of the ureter are rendered more tense, and are thus approximated towards each other (fig. 354).

279. URINARY BLADDER AND URETHRA.—Structure.—The mucous membrane of the bladder resembles that of the ureter; the upper layers of the stratified transitional epithelium are somewhat flattened (fig. 354). It is obvious that the form of the cells must vary with the state of distention or contraction in the bladder. [The mucous membrane and muscular coats are thicker than in the ureter. There are mucous glands in the mucous membrane, especially near the neck of the bladder.]

Sub-mucous Coat.—There is a layer of delicate fibrillar connective-tissue mixed with elastic fibres between the mucous and muscular layers.

[The **serous coat** is continuous with, and has the same structure as the peritoneum and it covers only the posterior and upper half of the organ.]

Musculature.—*Non-stripped* muscular fibres are arranged in bundles in several layers, an *external longitudinal* layer, best developed on the anterior and posterior surfaces, and an *inner circular* layer. [Between these two is an *oblique* layer.] There are other bundles of muscular fibres arranged in different directions. **Physiologically**, the musculature of the bladder represents a single or common hollow muscle, whose function when it contracts is to diminish uniformly the size of the bladder, and thus to expel its contents (§ 306).

The **blood-vessels** resemble those of the ureter. The **nerves** form a plexus, and are placed partly in the mucous membrane and partly in the muscular coat, and, like all the extra-renal parts of the urinary apparatus, are provided with **ganglia**, lying in the mucosa, sub-mucosa, and connected to each other by fibres (*Maier*). Ganglia occur in the course of the motor nerve-fibres in the bladder (*W. Wolff*). Their functions are **motor**, **sensory**, **excito-motor**, and **vaso-motor**. [Sympathetic nerve-ganglia also exist underneath the serous coat (*F. Darwin*).]

A too minute dissection of the several layers and bundles of the musculature of the bladder has given rise to erroneous inferences. Thus, we speak of a **detrusor urinæ**, which, however, consists chiefly of fibres running on the anterior and posterior surfaces, from the vertex to the fundus. There does not seem to be a special **sphincter vesicæ internus**; it is merely a thicker circular (6 to 12 mm.) layer of non-stripped muscle which surrounds the beginning of the urethra, and which, from its shape, helps to form the funnel-like exit of the bladder. Numerous muscular bundles, connected partly with the longitudinal and partly with the circular fibres of the bladder, exist, especially in the trigone, between the orifice of the ureters.

In the **female**, the urethra serves merely for the passage of urine. The mucous membrane consists of connective-tissue with many elastic fibres, and provided with papillæ. It is covered by stratified epithelium and contains several mucous glands (*Littre*). Outside this is a layer of longitudinal, smooth, muscular fibres, and outside this again a layer of circular fibres. Many elastic fibres exist in all the layers, which are traversed by numerous wide venous channels.

The proper **sphincter urethræ** is a *transversely striped* muscle subject to the will, and consists of completely circular fibres which extend downwards as far as the middle of the urethra, and partly of longitudinal fibres, which extend only on the posterior surface towards the base of the bladder, where they become lost between the fibres of the circular layer.

In the **male urethra**, the **epithelium** of the prostatic part is the same as that in the bladder; in the membranous portion it is stratified, and in the cavernous part the simple cylindrical form. The mucous membrane, under the epithelium itself, is beset with *papillæ*, chiefly in the posterior part of the urethra, and contains the mucous glands of *Littre*.

Non-stripped muscle occurs in the prostatic part arranged longitudinally, chiefly at the *colliculus seminalis*; in the membranous portion the direction of the fibres is chiefly circular, with a few longitudinal fibres intercalated; the cavernous part has a few circular fibres posteriorly, but anteriorly the muscular fibres are single and placed obliquely and longitudinally.

Closure of the Bladder.—The so called internal vesical sphincter of the anatomists, which consists of non-stripped muscle, is in reality an integral part of the muscular coat of the bladder, and surrounds the orifice of the urethra as far down as the prostatic portion, just above the *colliculus seminalis*. It is, however,

not the sphincter muscle. The proper **sphincter urethræ** (sph. vesicæ externus) lies below the latter. It is a completely circular muscle disposed around the urethra, close above the entrance of the urethra into the septum urogenitale at the apex of the prostate, where it exchanges fibres with the deep transverse muscle of the perinæum which lies under it.

Some longitudinal fibres, which run along the upper margin of the prostate from the bladder, belong to this sphincter muscle. Single transverse bundles passing forward from the surface of the neck of the bladder, the transverse bands which lie within the prostate, the apex of the colliculus seminalis, and a strong transverse bundle passing in front of the origin of the urethra into the substance of the prostate—all belong to the sphincter muscle (*Henle*). In the male urethra, the *blood-vessels* form a rich capillary plexus under the epithelium, below which is a wide-meshed *lymphatic* plexus.

[**Tonus of Sphincter Urethræ.**—Open the abdomen of a rabbit, ligature one ureter, tie a cannula in the other, and pour water into the bladder until it runs out through the urethra, which usually occurs under a pressure of 16 to 20 inches. If the spinal cord be divided between the fifth and seventh lumbar vertebræ, a column of 6 inches is sufficient to overcome the resistance of the sphincter, while section at the fourth lumbar vertebra has no effect on the height of the pressure. In such an animal the bladder becomes distended, but in one with its cord divided between the fifth and seventh lumbar vertebræ, there is incontinence of urine—in the former case because the excitomotor impulses are cut off from the centre (5 to 7 vert.), and in the latter because the tonus of the sphincter is destroyed (*Kupressow*). This tonus is denied by Landois and others.]

280. ACCUMULATION OF URINE—MICTURITION.—After emptying the bladder, the urine slowly collects again, the bladder being thereby gradually distended. [A healthy bladder may be said to be full when it contains 20 oz.] As long as there is a moderate amount of urine in the bladder, the elasticity of the elastic fibres surrounding the urethra, and that of the sphincter of the urethra (and in the male of the prostate), suffice to retain the urine in the bladder. This is shown by the fact that the urine does not escape from the bladder after death. If the bladder be greatly distended (1·5 to 1·8 litre), so that its apex projects above the pubes, the sensory nerves in its walls are stimulated and cause a feeling of a full bladder, while at the same time the urethral opening is dilated, so that a few drops of urine pass into the beginning of the urethra. Besides the subjective feeling of a full bladder, this tension of the walls of the bladder causes a *reflex* effect, so that the urinary bladder contracts periodically upon its fluid contents, and so do the sphincter of the urethra and the muscular fibres of the urethra, and thus the urethra is closed against the passage of these drops of urine. As long as the pressure within the bladder is not very high, the reflex activity of the transversely striped sphincter overcomes the other (as during sleep); but as the pressure rises and the distention increases, the contraction of the walls of the bladder overcomes the closure produced by the sphincter, and the bladder is emptied, as occurs normally in young children.

As age advances, the sphincter urethræ comes under the control of the will, so that it can be contracted voluntarily, as occurs in man when he forcibly contracts the bulbo-cavernosus muscle to retain urine in the bladder. The sphincter and usually contracts at the same time. The reflex activity of the sphincter may also be inhibited voluntarily, so that it may be completely relaxed. This is the condition when the bladder is emptied voluntarily.

Slight **movements**, confined to the bladder, occur during psychical or emotional disturbances (*e.g.*, anger, fear), [the bladder may be emptied involuntarily during a fright], after stimulation of sensory nerves, auditory impressions, restraining respiration, and by arrest of the heart's action. There are slight periodic variations coincident with variations in the blood-pressure. The contractions of the bladder cease after deep inspiration, and also during apnoea (*Mosso and Pellacani*). The excised bladder of the frog, and even portions free from ganglia, exhibit rhythmical contractions, which are increased by heat (*Pfalz*). [Ashdown found in dogs that the bladder exhibits regular rhythmical contractions, which were influenced by the degree of distention of the bladder, being most marked with moderate dilatation and least when the

bladder was feebly or over-distended. The contractions could be registered by means of a water-manometer communicating with the interior of the bladder.]

Nerves of micturition.—The nerves concerned in the retention and evacuation of the urine are :—1. The **motor nerves** of the sphincter urethræ, which lie in the pudendal nerve (anterior roots of the third and fourth sacral nerves). When these nerves are divided, as soon as the bladder becomes so distended as to dilate the urethral opening, the urine begins to trickle away (incontinence of urine). 2. The **sensory nerves** of the urethra, which excite these reflexes, leave the spinal cord by the posterior roots of the third, fourth, and fifth sacral nerves. Section of these nerves causes incontinence of urine. The **centre** for the reflex in dogs lies opposite the fifth, and in rabbits opposite the seventh lumbar vertebra (*Budge*). 3. Fibres pass from the cerebrum—those that convey voluntary impulses through the peduncles, and the anterior columns of the spinal cord (according to Mosso and Pellacani, through the posterior columns and the posterior part of the lateral columns), to the motor fibres of the sphincter urethræ. 4. The **inhibitory fibres** concerned in the reflex-inhibition of the sphincter urethræ take the same course (perhaps from the optic thalamus?) downwards through the cord to where the third, fourth, and fifth sacral nerves leave it. 5. Sensory nerves proceed from the urethra and bladder to the brain, but their course is not known. Some of the motor and sensory fibres lie for a part of their course in the sympathetic.

[Just as the rectum is supplied by two sets of nerve-fibres, so the bladder receives nerve-fibres, viz., from the sacral nerves. Stimulation of these nerves not only causes contraction of the longitudinal fibres of the rectum, but also contraction of the bladder, in which act the longitudinal muscular fibres of the bladder take the most active part. Stimulation of the hypogastric nerves coming from the upper lumbar and dorsal region cause chiefly contraction of the circular fibres of the bladder, as well as contraction of the circular fibres of the rectum.]

Transverse section of the spinal cord above where the nerves leave it, is always followed in the first instance by retention of urine, so that the bladder becomes distended. This occurs because—(1) the section of the spinal cord increases the reflex activity of the urethral sphincter; and (2), because the inhibition of this reflex can no longer take place. As soon, however, as the bladder becomes so distended, as in a purely mechanical manner to cause dilatation of the urethral orifice, then the urine trickles away, but the amount of urine which trickles out in drops is small. Thus the bladder becomes more and more distended, as the continuously distended walls of the organ yield to the increased tension, so that the bladder may become distended to an enormous extent. The urine very frequently becomes ammoniacal, accompanied by catarrh and inflammation of the bladder (§ 263).

[In dogs, with their cord divided at the last dorsal vertebra,—whereby the lumbar part of the cord is completely cut off from all volitional impulses,—after a time, *i.e.* when the cord has recovered, micturition takes place reflexly when the bladder is full. The reflex act may be excited by gentle stimulation of the skin round the anus or slight pressure on the abdomen (*Goltz*).]

Voluntary Micturition.—Observers are not agreed as to the mechanism concerned in emptying the bladder when it is only partially full. It is stated by some that a voluntary impulse passes from the brain along a cerebral peduncle, and the cord, to the anterior roots of the third and fourth sacral nerves, and partly through motor fibres from the second to the fifth lumbar nerves (especially the third), to act directly upon the smooth muscular fibres of the bladder. This is assumed, because electrical stimulation of any part of this nervous channel causes contraction of the bladder. This view, however, does not seem to be the true one. It is to be remembered that *Budge* showed that the sensory nerves of the wall of the bladder are contained in the first, second, third, and fourth sacral nerves, and also in part

in the course of the hypogastric plexus, whence they ultimately pass by the rami communicantes into the spinal cord.

According to Landois, the smooth musculature of the bladder cannot be excited directly by a voluntary impulse, but it is always caused to contract reflexly. If we wish to micturate when the urinary bladder contains a small quantity of urine, we first excite the sensory nerves of the opening of the urethra, either by causing contraction or relaxation of the sphincter urethræ, or by means of slight abdominal pressure, and thus force a little urine into the urethral orifice. This sensory stimulation causes a reflex contraction of the walls of the urinary bladder. At the same time, this condition is maintained voluntarily, by the action of the intracranial reflex-inhibitory centre of the sphincter urethræ. The centre for the reflex stimulation of the movements of the walls of the urinary bladder is placed somewhat higher in the spinal cord than that for the sphincter urethræ. In dogs, it is opposite the fourth lumbar vertebra (*Gianuzzi, Budge*).

[Two centres are assumed to exist in the cord, fig. 355, one the automatic (A.C.) at the segment corresponding to the second, third, and fourth sacral nerves, which maintains the tonic action of the sphincter; the other, a reflex centre (R.C.), is situated higher, and through it the detrusor urinæ is excited to contraction. Both centres are connected to and governed or controlled by a cerebral centre (C). The automatic centre is connected with the sphincter, and the other with the urine-expelling fibres. They are also connected with afferent fibres from the bladder and elsewhere. The afferent or sensory fibres are also connected with the brain. The automatic centre maintains the closure of the bladder, but if the latter be distended, different impulses proceeding from it reach the spinal centre, and it may be the cerebrum. The impulses reaching the automatic centre inhibit its action and those to the reflex centre excite it, so that the detrusor urinæ contracts. If the afferent impulses be powerful, a desire to urinate is excited, and voluntary impulses are excited which act upon the spinal centres as the afferent impulses do, and thus the act of urination is more easily accomplished.]

We may conceive a voluntary impulse to pass down special fibres to an inhibitory centre, which may either act directly on the motor centre, or possibly may send branches directly to the sphincter muscles.

Painful stimulation of sensory nerves causes reflex contraction of the bladder and evacuation of the urine (in children during teething). Reflex contraction of the bladder can be brought about in cats by stimulation of the inferior mesenteric ganglion. After section of all the nerves going to the bladder, hæmorrhage and asphyxia cause contraction by a direct effect upon the structures in the wall of the bladder. As yet no one has succeeded in exciting artificially the inhibitory centre in the brain for the sphincter muscle (*Sokowin and Kowalesky*).

It seems probable that, as in the case of the anal sphincter (§ 160), there is not a *continuous tonic* reflex stimulation of the sphincter urethræ; the reflex is excited each time by the contents. The sphincter vesicæ of the anatomists, which consists of smooth muscular tissue, does not seem to take part in closing the bladder. Budge and Landois found that, after removal of the transversely striped sphincter urethræ, stimulation of the smooth sphincter did not cause occlusion of the bladder, nor could L. Rosenthal or v. Wittich convince themselves of the presence of tonus in this muscle. Indeed, its very existence is questioned by Henle.

Changes of the Urine in the Bladder.—When the urine is retained in the bladder for a considerable time, according to Kaupp, there is an increase in the sodium chloride and a decrease in the urea and water. Urine which remains for a long time in the bladder is prone to undergo ammoniacal decomposition.

Absorption.—Many observers have shown that the mucous membrane of the bladder is capable of absorbing substances—potassium iodide and other soluble salts. [Ashdown has shown that poisons, such as watery solutions of strychnin, curare, eserine, emulsions of chloroform and ether, are absorbed when injected into the bladder of rabbits. In rabbits, KI injected into the

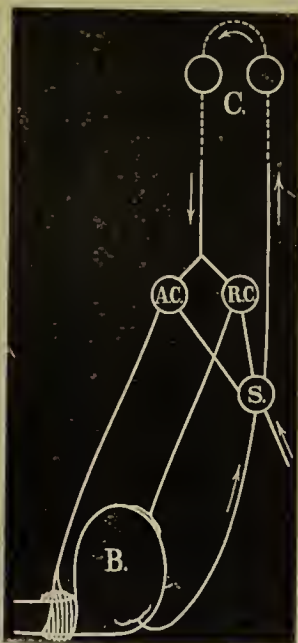


Fig. 355.

Scheme of micturition:—A.C., R.C., C., automatic, reflex, and cerebral centres; B., bladder; S., sensory centre acted on by afferent impulses.

bladder through a catheter was found in the urine obtained from the divided ureters. Water and urica are also absorbed—the latter in larger proportion than the former.]

As the ureters enter near the base of the bladder, the last-secreted urine is always lowest. If a person remain perfectly quiet, strata of urine are thus formed, and the urine may be voided so as to prove this (*Edlefson*).

The pressure within the bladder, when in the supine position = 13 to 15 centimetres of water. Increase of the intra-abdominal pressure (by inspiration, forced expiration, coughing, bearing down) increases the pressure within the bladder. The erect posture also increases it, owing to the pressure of the viscera from above (*Schaltz, Dubois*). [James obtained 4 to 4.5 inches Hg as the highest expulsive power of the bladder, including the abdominal pressure, voluntary and involuntary. In paraplegia, where there is merely the expulsive power of the bladder, he found 20 to 30 inches of water.]

[**Hydronephrosis** occurs when the ureters and pelvis of the kidney become dilated, owing to partial and gradual obstruction of the outflow of urine from the ureters: if the obstruction become complete, there is cessation of the urinary secretion. James has shown that the bladder remains contracted for several seconds after it is emptied, and this is specially the case in irritable bladder; so that this condition may also give rise to hydronephrosis by damming up the urine in the ureters.]

Rapidity of Micturition.—The amount of urine voided at first is small, but it increases with the time, and towards the end of the act it again diminishes. In men, the last drops of urine are ejected from the urethra by voluntary contractions of the bulbo-cavernosus muscle. Adult dogs increase the stream rhythmically by the action of this muscle.

281.—RETENTION AND INCONTINENCE OF URINE.—Retention of urine or ischuria occurs:—1. When there is obstruction of the urethra, from foreign bodies, concretions, stricture, swelling of the prostate. 2. Paralysis or exhaustion of the musculature of the bladder; the latter sometimes occurs after delivery, in consequence of the pressure of the child against the bladder. 3. After section of the spinal cord (p. 540). 4. Where the voluntary impulses are unable to act upon the inhibitory apparatus of the sphincter urethræ reflex, as well as when the sphincter urethræ reflex is increased.

Incontinence of urine (stillicidium urinæ) occurs in consequence of—1. Paralysis of the sphincter urethræ. 2. Loss of sensibility of the urethra, which of course abolishes the reflex of the sphincter. 3. Trickling of the urine is a secondary consequence of section of the spinal cord, or of its degeneration.

Strangury is an excessive reflex contraction of the walls of the bladder and sphincter, due to stimulation of the bladder and urethra; it is observed in inflammation, neuralgia [and after the use of some poisons, *e.g.*, cantharides].

Enuresis nocturna, or involuntary emptying of the bladder at night, may be due to an increased reflex excitability of the wall of the bladder, or weakness of the sphincter.

282. COMPARATIVE AND HISTORICAL.—Amongst vertebrates, the urinary and genital organs are frequently combined, except in the osseous fishes. The Wolffian bodies, which act as organs of excretion during the embryonic period, remain throughout life in fishes and amphibians and continue to act as such. **Fishes.**—The *myxinoïds* (cyclostomata) have the simplest kidneys; on each side is a long ureter with a series of short-stalked glomeruli with capsules arranged along it. Both ureters open at the genital pore. In the other fishes, the kidneys lie often as elongated compact masses along both sides of the vertebral column. The two ureters unite to form a urethra, which always opens behind the anus, either united with the opening of the genital organs, or behind this. In the sturgeon and hag-fish, the anus and orifice of the urethra together form a cloaca. Bladder-like formations, which, however, are morphologically homologous with the urinary bladder of mammals, occur in fishes, either on each ureter (ray, hag-fish), or where both join. In amphibians, the vasa efferentia of the testicles are united with the urinary tubules; the duct in the frog unites with the one on the other side, and both conjoined open into the cloaca, whilst the capacious *urinary bladder* opens through the anterior wall of the cloaca. From reptiles upwards, the kidney is no longer a persistent Wolffian body, but a new organ. In reptiles, it is usually flattened and elongated; the ureters open singly into the cloaca. Snarrians and tortoises have a urinary bladder. In birds, the isolated ureters open into the urogenital sinus, which opens into the cloaca, internal to the excretory ducts of the genital apparatus. The urinary bladder is always absent. In mammals, the kidneys often consist of many lobules, *e.g.*, dolphin, ox.

Amongst invertebrates, the mollusca have excretory organs in the form of canals, which are provided with an outer and inner opening. In the mussel this canal is provided with a sponge-like organ, often with a central cavity, and consisting of ciliated secretory cells, placed at the base of the gills (organ of Bojanus). In gasteropods, with analogous organs, uric acid has been found. Insects, spiders, and centipedes have the so-called Malpighian vessels, which are excretory organs partly for uric acid and partly for so-called bile. These vessels are long tubes, which open into the first part of the large intestine. In crabs, blind tubes connected with the intestinal tube perhaps have the same functions. The vermes also have renal organs.

Historical.—Aristotle directed attention to the relatively large size of the human bladder—he named the ureters. Massa (1552) found lymphatics in the kidney. Eustachius († 1580) ligatured the ureters and found the bladder empty. Cusanus (1565) investigated the colour and weight of the urine. Rousset (1581) described the muscular nature of the walls of the bladder. Vesling described the trigone (1753). The first important chemical investigations on the urine date from the time of van Helmont (1644). He isolated the solids of the urine, and found among them common salt; he ascertained the higher specific gravity of fever-urine, and ascribed the origin of urinary calculi to the solids of the urine. Scheele (1766) discovered uric acid and calcium phosphate; Arand and Kunckel, phosphorus; Rouelle (1773), urea; and it got its name from Fourcroy and Vauquelin (1799). Berzelius found lactic acid; Seguin, albumin in pathological urine; Liebig, hippuric acid; Heintz and v. Pettenkofer, kreatin and kreatinin; Wollaston (1810), cystin. Mareet found xanthin; and Lindbergson, magnesie carbonate.

Functions of the Skin.

283. STRUCTURE OF THE SKIN, HAIRS, AND NAIL.—The skin (3·3 to 2·7 mm. thick; specific gravity, 1057) consists of—

[1. The epidermis;

2. The chorium, or *cutis vera*, with the papillæ (fig. 356).]

The epidermis (0·08 to 0·12 mm. thick) consists of many layers of stratified

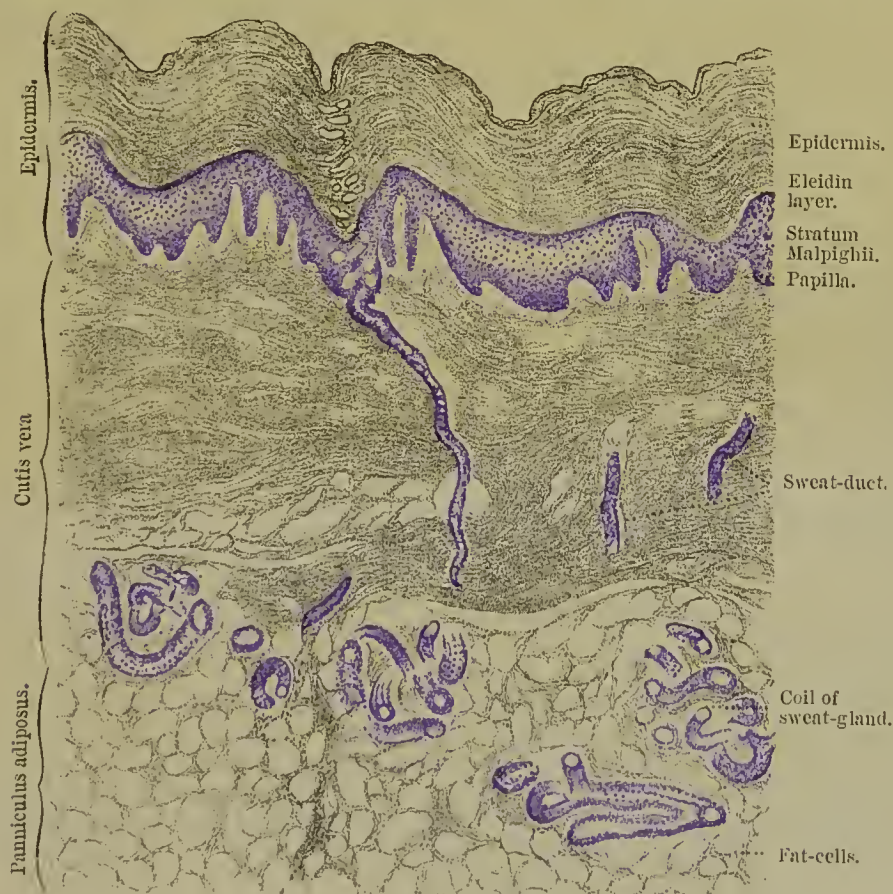


Fig. 356.

Vertical section of the human skin.

epithelial cells united to each other by cement substance (figs. 356, 357, 358). The superficial layers—**stratum corneum**—consist of several or many layers of

dry horny non-nucleated squames, which swell up in solution of caustic soda (fig. 358, E). [It is always thickest where intermittent pressure is applied, as on the sole of the foot and palm of the hand.] The next layer is the **stratum lucidum**, which is clear and transparent in a section of skin, hence the name, and consists of a few compact layers of clear cells with vestiges of nuclei. [The cells are two or three deep, are without granules, and do not stain readily.] Under this is the **rete mucosum** or rete Malpighii (fig. 358, d), consisting of many layers of nucleated protoplasmic epithelial cells which contain pigment in the dark races,

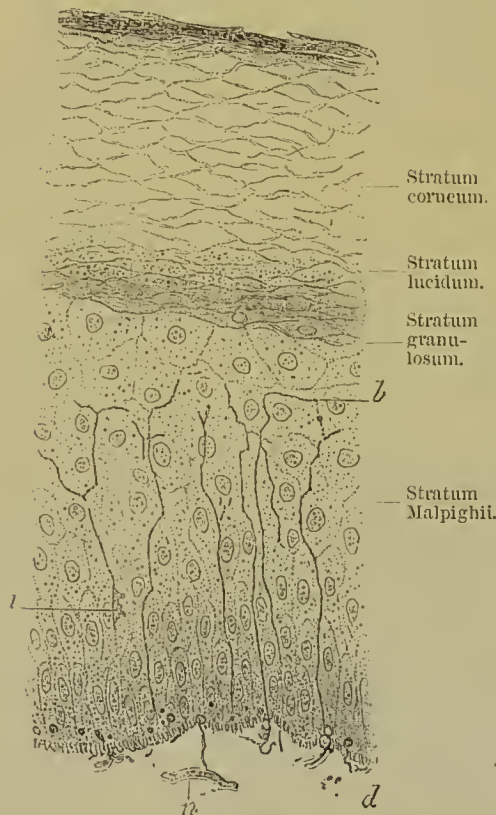


Fig. 357.

Vertical section of the human epidermis; the nerve-fibrils, *n*, *b*, stained with gold chloride.

and in the skin of the scrotum, and around the anus. [The superficial cells are more fusiform—at least they appear fusiform in section—and contain granules which stain deeply with carmine and osmic acid, and they are devoid of prickles. They constitute, 3, the **stratum granulosum**. In these cells the formation of keratin is about to begin, and they contain two sets of granules—the intra-cellular, hyaline, albumenoid granules of Waldeyer, which stain with logwood, and the **eleidin** granules of Ranvier, which seem to be allied to fatty bodies, and are readily stained by alkanet. All corneous structures contain similar granules in the area where the cells are becoming corneous. Then follow several layers of more or less polyhedral cells, constituting the **stratum Malpighii**, softer and more plastic in their nature, and exhibiting the characters of so-called “prickle cells” (fig. 358, R). [The spaces between the fibrils connecting adjacent cells are lymph-spaces.] The deepest layers of cells are more or less columnar, and the cells are placed vertically upon the papillæ and are provided with spherical nuclei. Granular **leucocytes** or wandering cells are sometimes found between these cells. The rete Malpighii dips down between adjacent papillæ and forms inter-

papillary processes. According to Klein, a delicate **basement membrane** separates the epidermis from the true skin.] The superficial layers of the epidermis are continually being thrown off, while new cells are continually being formed in the deeper layers of the skin by proliferation of the cells of the rete Malpighii, so that many of the cells may exhibit mitosis. There is a gradual change in the microscopic and chemical characters of the cells from the deepest to the superficial layers of the epidermis. [In a vertical section of the skin stained with picro-carmin, the S. granulosum is deeply stained red, and is thus readily distinguished amongst the other layers of the epidermis.]

Epidermis (fig. 357),	{	(1) Stratum corneum,	{	<i>Cuticle.</i>
		(2) Stratum lucidum,		
		(3) Stratum granulosum,	{	<i>Rete</i>
		(4) Stratum Malpighii,		
				<i>Mucosum.</i>

No pigment is formed within the epidermis itself [but in the coloured races

pigment-granules of **melanin** exist in the cells of the deepest layers of the stratum Malpighii]; when it is present, it is carried by leucocytes from the subcutaneous tissue (*Riehl, Ehrmann, Aebly*). This explains how it is that a piece of white skin, transplanted to a negro, becomes black (*Kary*).



Fig. 358.

I, Vertical section of the skin, with a hair and sebaceous gland, T. Epidermis and chorium shortened—1, outer; 2, inner fibrous layer of the hair-follicle; 3, its hyaline layer; 4, outer root-sheath; 5, Huxley's layer of the inner root-sheath; 6, Henle's layer of the same; p, root of the hair, with its papilla; A, arrector pili muscle; C, chorium; a, subcutaneous fatty tissue; b, epidermis (horny layer); d, rete Malpighii; g, blood-vessels of papillæ; v, lymphatics of the same; h, horny or corneous substance; i, medulla or pith; k, epidermis or cuticle of hair; K, coil of sweat-gland; E, epidermal scales (seen from above and *en face*) from the stratum corneum; R, prickle cells from the rete Malpighii; n, superficial, and m, deep cells from the nail; H, hair magnified; e, cuticle; c, medulla, with cells; f, fusiform fibrous cells of the substance of the hair; x, cells of Huxley's layer; l, those of Henle's layer; S, transverse section of a sweat-gland from the axilla; a, smooth muscular fibres surrounding it; t, cells from a sebaceous gland, some of them containing granules of oil.

[Herxheimer has described some peculiar "spirals" in the epidermis. They seem to be due to coagulation of a proteid.]

The **chorium** (fig. 358, I, C) is beset over its entire surface by numerous (0.5

to 0.1 mm. high) **papillæ** (figs. 356, 358), the largest being upon the volar surface of the hand and foot, on the nipple and glans penis. Most of the papillæ contain a looped **capillary** (*g*), while in certain regions some of them contain a **touch-corpuscle** (fig. 359, *a*). The papillæ are disposed in groups, whose arrangement varies in different parts of the body. In the palm of the hand and sole of the foot they occur in rows, which are marked out by the existence of delicate furrows on the surface visible to the naked eye. The chorium consists of a dense network of bundles of white fibrous tissue mixed with a network of **elastic fibres**, which are

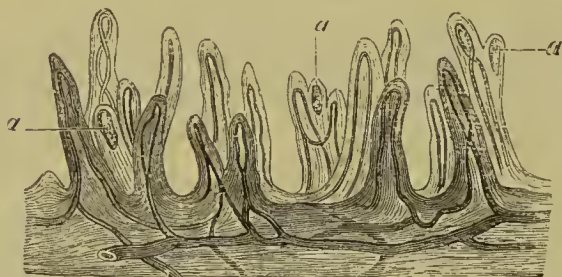


Fig. 359

Papillæ of the skin, epidermis removed, blood-vessels injected; some contain a Wagner's touch-corpuscle, *a*, the others a capillary loop.

more delicate in the papillæ. In silversmiths the elastic fibres are blackened by the partial deposition of reduced silver, and the same obtains in those who take silver nitrate in such quantity as to produce argyria. The connective-tissue contains many connective-tissue corpuscles and numerous leucocytes. The deeper connective-tissue layers of the chorium gradually pass into the **subcutaneous tissue**, where they form a trabecular arrangement of bundles, leaving between them elongated rhomboidal spaces filled for the most part with groups of **fat-cells** (figs. 356, 358, *a*, *a*). [In microscopic sections, after the action of alcohol, the fat-cells not unfrequently contain crystals of **margarin** (fig. 295).] The long axis of the rhomb corresponds to the greater tension of the skin at that part (*C. Langer*). In some situations the subcutaneous tissue is devoid of fat [penis, eyelids]. In many situations, the skin is fixed by solid fibrous bands to subjacent structures, as fasciæ, ligaments or bones (*tenacula cutis*); in other parts, as over bony prominences, bursæ partially lined with endothelium and filled with synovia-like fluid, occur.

Smooth muscular fibres occur in the chorium in certain situations on extensor surfaces (*Neumann*); nipple, areola mammæ, prepuce, perinæum, and in special abundance in the tunica dartos of the scrotum.

[**Guanin in the Skin.**—The skin of many amphibians and reptiles contain brown or black pigment-granules, and other granules of a white, silvery, or chalky appearance. Ewald and Krukenberg have shown that the latter consist of guanin, and that this substance is very widely diffused in the skin of fishes, amphibians, and reptiles. **Test**:—Select a piece of skin from the belly of a frog; place it in a porcelain capsule as for the murexide test; add concentrated nitric acid, and heat to dryness, when a yellow residue is obtained; on adding a drop of caustic soda a red colour is struck. The yellow residue gives no reaction with ammonia. If to the fluid more water be added, and it be then heated, distributed over the surface of the capsule, and cooled by blowing upon it, various shades of purple and violet are obtained.]

The **nails** (specific gravity 1.19) consist of numerous layers of solid, horny, homogeneous, epidermal, or nail-cells, which may be isolated with a solution of caustic alkali, when they swell up and exhibit the remains of an elongated nucleus (fig. 358, *n*, *m*). The whole under-surface of the nail rests upon the **nail-bed**; the lateral and posterior edges lie in a deep groove, the **nail-groove** (fig. 360, *e*). The chorium under the nail is covered throughout its entire extent by longitudinal rows of **ridges** (fig. 360, *d*). Above this there lies, as in the skin, many layers of prickly cells like those in the rete Malpighii (fig. 358, *d*), and above this again is the substance of the nail (fig. 360, *a*). [The stratum granulosum is rudimentary in the nail-bed. The substance of the nail represents the stratum lucidum, there being no stratum corneum (*Klein*).] The posterior part of the nail-groove and the half moon, brighter part or **lunule**, form the **root** of the nail. They are, at the

same time, the **matrix**, from which growth of the nail takes place. The lunule is present in an isolated nail, and is due to diminished transparency of the posterior part of the nail, owing to the special thickness and uniform distribution of the cells of the rete Malpighii (*Toldt*).

Growth of the Nail.—According to Unna, the matrix extends to the front part of the lunule. The nail grows continually from behind forwards, and is formed by layers secreted or formed by the matrix. These layers run parallel to the surface of the matrix. They run obliquely from above and behind, downwards and forwards, through the thickness of the substance of the nail. The nail is of the same thickness from the anterior margin of the lunule forwards to its free margin. Thus the nail does not grow in thickness in this region. In the course of a year the fingers produce about 2 grms. of nail substance, and relatively more in summer than in winter.

Development.—1. From the second to the eighth month of foetal life, the position of the nail is indicated by a partial but marked horny condition of the epidermis on the back of the first phalanx, the “**eponychium**.” The remainder of this substance is represented during life by the normally formed epidermal layer, which separates the future nail from the surface of the furrow. 2. The future nail is formed under the eponychium, with its first nail-cells still in front of the nail-groove; then the nail grows and pushes forward towards the groove. At the seventh month, the nail (itself covered by the eponychium) covers the whole extent of the nail-bed. 3. When, at a later period, the eponychium splits off, the nail is uncovered. After birth the ridges are formed on the bed of the nail, while simultaneously the matrix passes backwards to the most posterior part of the groove (*Unna*).

Absence of Hairs.—The whole of the skin, with the exception of the palmar surface of the hand, sole of the foot, dorsal surface of the third phalanx of the fingers and toes, outer surface of the eyelids, glans penis, inner surface of the prepuce, and part of the labia, is covered with hairs, which may be strong or fine (*lanugo*).

A **Hair** (specific gravity 1.26) is fixed by its lower extremity (root) in a depression of the skin or a **hair-follicle** (fig. 358, I, *p*) which passes obliquely

through the thickness of the skin, sometimes as far as the subcutaneous tissue. The structure of a hair-follicle is the following:—1. The **outer fibrous layer** (figs. 358, 1, 357), composed of interwoven bundles of connective-tissue, arranged for the most part longitudinally, and provided with numerous blood-vessels and nerves. [It is just the connective-tissue of the surrounding chorion.] 2. The **inner fibrous layer** (figs. 358, 2, 361) consists of a layer of fusiform cells (? smooth muscular fibres) arranged circularly. [It does not extend throughout the whole length

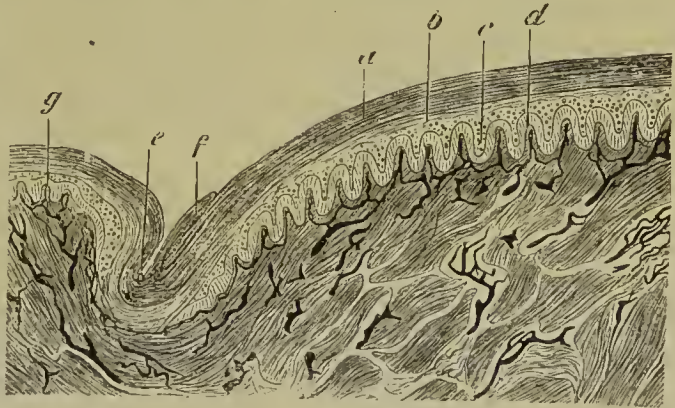


Fig. 360.

Transverse section of one-half of a nail. *a*, nail-substance; *b*, more open layer of cells of the nail-bed; *c*, stratum Malpighii of the nail-bed; *d*, transversely divided ridges; *e*, nail-groove; *f*, horny layer of *c* projecting over the nail; *g*, papillae of the skin on the back of the finger.

of the follicle.] 3. Inside this layer is a transparent, hyaline, glass-like **basement membrane** (fig. 358, 3, 361), which ends at the neck of the hair-follicle; while above it is continued as the basement membrane which exists between the epidermis and chorion (?). In addition to these coverings, a hair-follicle has epithelial coverings which must be regarded in relation to the layers of the epidermis. Immediately within the glass-like membrane is the **outer root-sheath** (figs. 358, 4, 361, 362), which consists of so many layers of epithelial cells that it forms a conspicuous covering. It is, in fact, a direct continuation of the stratum Malpighii, and consists of many layers of soft cells, the cells of the outer layer

being cylindrical. Towards the base of the hair-follicle it becomes narrower, and is united to, and continuous with, the cells of the root of the hair itself, at least in fully developed hairs. The horny layer of the epidermis continues to retain its properties as far down as the orifice of the sebaceous follicle; below this point, however, it is continued as the **inner root-sheath**. This consists of (1) a single layer of elongated, flat, homogeneous, non-nucleated cells (figs. 358, 6, 361, *f*—*Henle's layer*) placed next and within the outer root-sheath. Within this lies (2) *Huxley's layer* (figs. 358, 5, 361, *g*), consisting of nucleated elongated polygonal cells (fig. 358, *x*, and 3), while the *cuticle* of the hair-follicle is composed of cells analogous to those of the surface of the hair itself. Towards the bulb of the hair these three layers become fused together.

[Coverings of a hair-follicle arranged from without inwards—

- | | | |
|-----------------------------------|---|-------------------|
| 1. Fibrous layers, | { (a) Longitudinally arranged fibrous tissue. | |
| | { (b) Circularly arranged spindle cells. | |
| 2. Glass-like (hyaline) membrane. | | |
| 3. Epithelial layers. | { (a) Outer root-sheath. | { Henle's layer. |
| | { (b) Inner root-sheath. | { Huxley's layer. |
| | { (c) Cuticle of the hair. | |
| 4. The hair itself. | | |

The **arrector pili muscle** (fig. 358, A) is a fan-like arrangement of a layer of smooth muscular fibres, attached below to the side of a hair-follicle and extending towards the surface of the chorium; as it stretches obliquely upwards, it subtends the obtuse angle formed by the hair-follicle and the surface of the skin, [or, in other words, it forms an acute angle with the hair-follicle, and between it and the follicle lies the **sebaceous gland**]. When these muscles contract, they raise and erect the hair-follicles, producing the condition of **cutis anserina** or *gooseskin*. As the sebaceous gland lies in the angle between the muscle and the hair-follicle, contraction of the muscle compresses the gland and favours the evacuation of the sebaceous secretion. It also compresses the blood-vessels of the papilla (*Unna*).

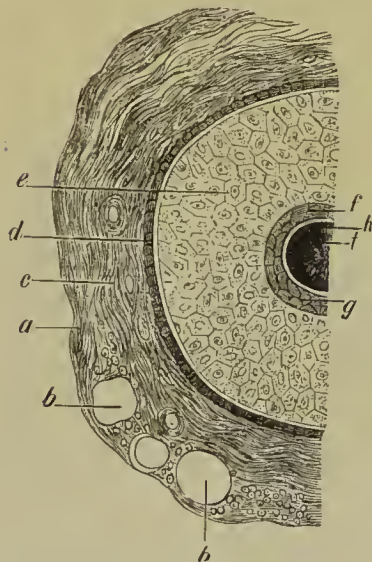


Fig. 361.

Transverse section of a hair and its follicle. *a*, outer fibrous coat, with *b*, blood-vessels; *c*, inner circularly disposed layer; *d*, glass-like layer; *e*, outer, *f*, *g*, inner, root-sheath; *f*, outer layer of the same (Henle's sheath); *g*, inner layer of the same (Huxley's sheath); *h*, cuticle; *l*, hair.

The hair with its large bulbous extremity—**hair-bulb**—sits upon, or rather embraces, the **papilla**. It consists of (1) the *narrow* or **medulla** (fig. 358, *i*), which is absent in woolly hair and in the hairs formed during the first year of life. It is composed of two or three rows of cubical cells (*H*, *c*). (2) Outside this lies the thicker **cortex** (*h*), which consists of elongated, rigid, horny, fibrous cells (*H*, *f*, *f*), while in and between these cells lie the pigment granules of the hair. (3) The surface of the hair is covered with a **cuticle** (*h*), which consists of imbricated layers of non-nucleated squames.

[**Nerves**.—Numerous nerve-fibres are distributed in the hair-follicles (§ 424).]

Grey Hair.—When the hair becomes *grey*, as in old age, this is due to defective formation of pigment in the cortical part. The silvery appearance of white hair is increased when small air-cavities are developed, especially in the medulla, and to a less extent in the cortex, where they reflect the light. Landois records a case of the hair becoming *suddenly* grey, in a man whose hair became grey during a single night, in the course of an attack of delirium tremens. Numerous air-spaces

were found throughout the entire marrow of the (blond) hairs, while the hair-pigment still remained.

[Blood-Pigment in Hairs.]—The feelers of albino rabbits contain blood-pigment in some part of their substance (*Sig. Mayer*).]

Development of Hair.—According to Kölliker, from the 12th to 13th week of intra-uterine life, solid finger-like processes of the epidermis are pushed down into the chorion. The process becomes flask-shaped, while the central cells of the cylinder become elongated, and form a conical body, arising as it were from the depth of the recess. It soon differentiates into an inner darker part, which becomes the hair, and a thinner, clearer layer covering the former, the inner root-sheath. The outer cells, *i.e.*, those lying next the wall of the sac, form the outer root-sheath. Outside this again the fibrous tissue of the chorion forms a rudimentary hair-follicle, while one of the papillæ grows up against it, indents it, and becomes embraced by the bulb of the hair. This is the hair papilla, which contains a loop of blood-vessels. The cells of the bulb of the hair proliferate rapidly, and thus the hair grows in length. The point of the hair is thereby gradually pushed upwards, pierces the inner root-sheath, and passes obliquely through the epidermis. The hairs appear upon the forehead at the 19th week; at the 23rd to 25th week the lanugo hairs appear free, and they have a characteristic arrangement on different parts of the body.

Physical Properties.—Hair has very considerable elasticity (stretching to 0.33 of its length), considerable cohesion (carrying 3 to 5 lbs.), resists putrefaction for a long time, and is highly hygroscopic. The last property is also possessed by epidermal scales, as is proved by the pains that occur in old wounds and sears during damp weather.

Growth of a hair occurs by proliferation of the cells on the surface of the hair papilla, these cells representing the matrix of the hair. Layer after layer is formed, and gradually the hair is raised higher within its follicle.

Change of the Hair.—According to one view, when the hair has reached its full length, the process of formation on the surface of the hair papilla is interrupted; the root of the hair is raised from the papilla, becomes horny, remains almost devoid of pigment, and is gradually more and more lifted upwards from the surface of the papilla, while its lower bulbous end becomes split up like a brush. The lower empty part of the hair-follicle becomes smaller, while on the old papilla a new formation of a hair begins, the old hair at the same time falling out (*Unna*). According to Stieda, the old papilla disappears, while a new one is formed in the hair-follicle, and from it the new hair is developed. According to Kölliker, again, both processes obtain.

[Erectile Hairs.]—The vibrissæ or feelers in the snout of some animals are really organs of touch, and in each hair-follicle is a large blood-sinus.]

[Chemistry.]—In the horny epithelium the protoplasm is replaced by keratin, which belongs to the group of the albumenoids (§ 250, 3) and contains sulphur, which is but loosely combined, for on boiling hairs with alkalis the sulphur is liberated. It is also the chief constituent of hairs, hoof, and feathers, while a similar body, neuro-keratin, is found in nervous structures. The quantity of sulphur in keratin is about 3–5 per cent. Hairs on being burned yield 5–70 per 1000 of ash, composed of 250 alkaline sulphates, 140 calcium sulphate, 100 iron oxide, and 400 parts of silicic acid. As a rule, dark hairs yield more iron than blond hairs.]

The colour of the skin in the coloured races, and the black or brown colour of hair in general, is due to melanin (p. 472). There seem to be several varieties of this pigment, but that of

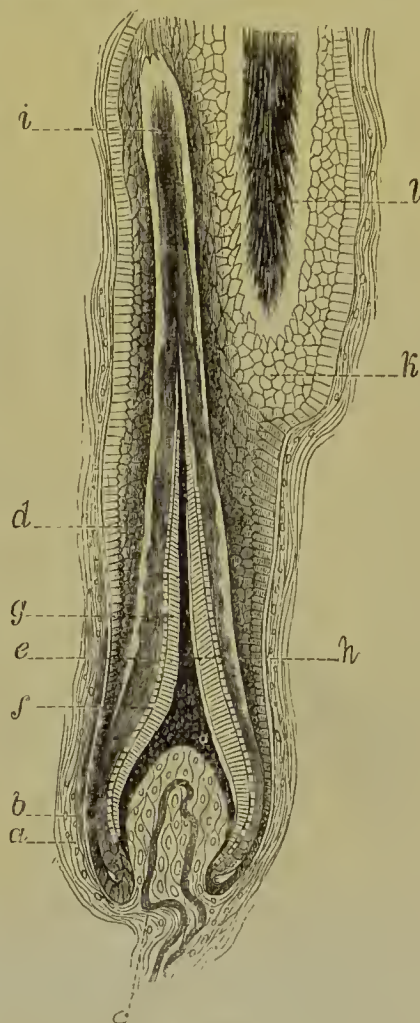


Fig. 362.

Section of a hair-follicle while a hair is being shed. *a*, outer and middle sheaths of hair-follicle; *b*, hyaline membrane; *c*, papilla, with a capillary; *d*, outer, *e*, inner root-sheath; *f*, cuticle of the latter; *g*, cuticle of the hair; *h*, young non-medullated hair; *i*, tip of new hair; *j*, hair-knob of the shed hair, with *k*, the remainder of the cast-off outer root-sheath.

human hair contains rather less nitrogen and more sulphur than some of the others. It does not contain iron.]

284. THE GLANDS OF THE SKIN.—The **sebaceous glands** (fig. 358, 1, T) are simple acinous glands, which open by a duct into the hair-follicles of large hairs near their upper part; in the case of small hairs, the latter may project from the duct of the gland (fig. 363). In some situations the ducts of the glands open free upon the surface, *e.g.*, the glands of labia minora, glans, prepuce (Tyson's glands), and the red margins of the lips. The largest glands occur in the nose and in the labia; they are absent only from the vola manus and planta pedis. The oblong alveoli of the gland consist of a basement membrane lined with small polyhedral nucleated granular secretory cells (fig. 358, *t*). Within this are other polyhedral cells, whose substance contains numerous oil-globules; the cells become more fatty towards the centre of the alveolus. The cells lining the duct are continuous with those of the outer root-sheath. The detritus formed by the fatty metamorphosis of the cells constitutes the **sebum** or sebaceous secretion.

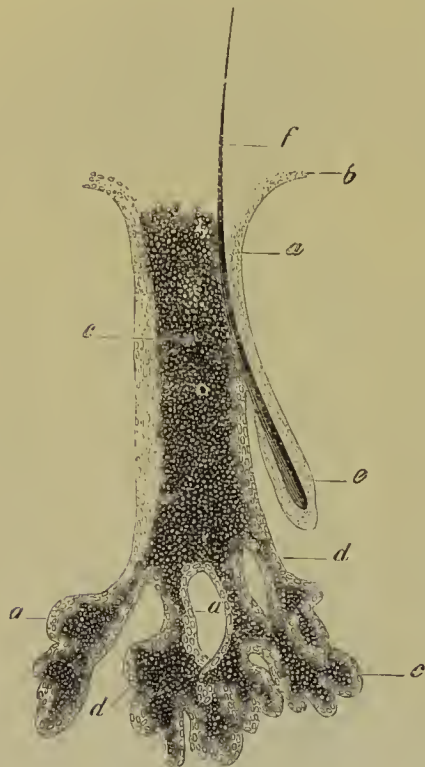


Fig. 363.

Sebaceous gland, with a lanugo hair. *a*, granular epithelium; *b*, rete Malpighii continuous with *a*; *c*, fatty cells and free fat; *d*, acini; *e*, hair-follicle, with a small hair, *f*.

mouth (fig. 356). The glands are very numerous and large in the palm of the hand, sole of the foot, axilla, forehead, and around the nipple; few on the back of the trunk; and are absent on the glans, prepuce, and margin of the lips. The **circumanal glands** and the **ceruminous glands** of the external auditory meatus, and **Moll's glands**, which open into the hair-follicles of the eyelashes, are modifications of the sweat-glands.

Each gland-tube consists of a basement membrane lined by cells; the **excretory** part or **sweat-canal** of the tube is lined by several layers of cubical cells, whose surface is covered by a delicate cuticular layer, a small central lumen being left. Within the coil the structure is different. The first part of the coil resembles the above, but as the coil is the true **secretory part** of the gland, its structure differs from the sweat-canal. This, the so-called *distal* portion of the tube, is lined by a single layer of moderately tall clear nucleated cylindrical epithelium (fig. 358, S), often containing oil-globules. Smooth muscular fibres are arranged longitudinally along the tube in the large glands (fig. 358, S, *a*). There is a distinct lumen present in the tube. As the duct passes through the epidermis, it winds its way

[If the "oil or eoeeygeal-gland" of a duck be removed, it is found that, when the animal is submerged, it takes up between its feathers about the same amount of water as an intact duct; but it retains 2 to 2½ times as much water in its feathers (Max Joseph).]

The **sweat-glands** (figs. 356, 358, I, *k*), sometimes called **sudoriparous glands**, consist of a long blind tube, whose lower end is arranged in the form of a coil placed in the areolar tissue under the skin, while the somewhat smaller upper end or excretory portion winds in a vertical, slightly wave-like manner, through the chorion, and in a cork-screw or **spiral manner** through the epidermis, where it opens with a free, somewhat trumpet-shaped,

between the epidermal cells without any independent membrane lining it (*Heynold*). A network of **capillaries** surrounds the coil. Before the arteries split up into capillaries, they form a true rete mirabile around the coil (*Brücke*). This is comparable to the glomerulus of the kidney, which may also be regarded as a rete mirabile. Numerous **nerves** pass to form a plexus, and terminate in the glands (*Tomsa*).

The total number of sweat-glands is estimated by Krause at $2\frac{1}{2}$ millions, which gives a secretory surface of nearly 1000 square metres. *These glands secrete sweat.* Nevertheless, an oily or fatty substance is often mixed with the sweat. In some animals (glands in the sole of the foot of the dog, and in birds) this oily secretion is very marked.

Numerous **lymphatics** occur in the cutis; some arise by a blind end, and others from loops within the papilla on a plane lower than the vascular capillary. [These open into more or less horizontal networks of tubular lymphatics in the cutis, and these again into the wide lymphatics of the subcutaneous tissue, which are well provided with valves.] Special lymphatic spaces are disposed in relation with the hair-follicles and their glands (*Neumann*), [and also with the fat (*Klein*). The lymphatics of the skin are readily injected with Berlin blue by the puncture method].

[The **blood-vessels** of the skin are arranged in several systems. There is a superficial system, from which proceed the capillaries for the papillæ. There is a deeper system of vessels which supplies special blood-vessels to (a) the fatty tissue; (b) the hair-follicles, each of which has a special vascular arrangement of its own, and in connection with this each sebaceous gland receives a special artery; (c) an artery goes also to each coil of a sweat-gland, where it forms a dense plexus of capillaries (*Tomsa*).]

285. THE SKIN AS A PROTECTIVE COVERING.—The subcutaneous fatty tissue fills up the depressions between adjoining parts of the body and covers projecting parts, so that a more rounded appearance of the body is thereby obtained. It also acts as a soft elastic pad and protects delicate parts from external pressure (sole of the foot, palm of the hand), and it often surrounds and protects blood-vessels, nerves, &c. It is a bad conductor of heat, and thus acts as one of the factors regulating the radiation of heat (§ 214, II., 4), and, therefore, the temperature of the body. The epidermis and cutis vera also act in the same manner (§ 212). Klug found that the heat-conduction is less through the skin and subcutaneous fatty tissue than through the skin alone; the epidermis conducts heat less easily than the fat and the chorium.

The solid, elastic, easily movable cutis affords a good *protection against external, mechanical injuries*; while the dry, impermeable, horny epidermis, devoid of nerves and blood-vessels, affords a further protection against the absorption of poisons, and at the same time it is capable of resisting, to a certain degree, thermal and even chemical actions. A thin layer of fatty matter protects the free surface of the epidermis from the macerating action of fluids, and from the disintegrating action of the air. The epidermis is important in connection with the *fluids of the body*. It exerts pressure upon the cutaneous capillaries, and to a limited extent, prevents too great diffusion of fluid from the cutaneous vessels. Parts of the skin devoid of epidermis are red and always moist. When dry, the epidermis and the epidermal appendages are bad conductors of electricity (§ 326). Lastly, the existence of uninjured epidermis prevents adjoining parts from growing together.

As the epidermis is but slightly extensible it is stretched over the folds and papillæ of the cutis vera, which becomes level when the skin is stretched, and the papillæ may even disappear with strong tension (*Lewinski*).

286. CUTANEOUS RESPIRATION: SEBUM—SWEAT.—The skin, with a surface of more than $1\frac{1}{2}$ square metre, has the following **secretory** functions:—

1. The **respiratory excretion**;
2. The **secretion of sebaceous matter**; and
3. The **secretion of sweat**.

[Besides this the skin is **protective**, contains **sense-organs**, is largely concerned in **regulating the temperature**, and may be concerned in **absorption**.]

1. **Respiration by the skin** has been referred to (§ 130). The organs concerned are the tubes of the sweat-glands, moistened as they are with fluids, and surrounded by a rich network of capillaries. It is uncertain whether or not the skin gives off a small amount of N or ammonia. Röhrig made experiments upon an arm placed in an air-tight metal box. According to him, the amount of CO₂ and H₂O excreted is subject to certain daily variations; it is increased by digestion, increased temperature of the surroundings, the application of cutaneous stimuli, and by impeding the pulmonary respiration. The exchange of gases also depends upon the vascularity of certain parts of the skin, while the cutaneous absorption of O also depends upon the number of coloured corpuscles in the blood.

In frogs and other amphibians, with a thin, always moist epidermis, the cutaneous respiration is more considerable than in warm-blooded animals. In winter, in frogs, the skin alone yields $\frac{3}{4}$ of the total amount of CO₂ excreted; in summer $\frac{2}{3}$ of the same (*Bidder*); thus, in these animals it is a more important respiratory organ than the lungs themselves.

Suppression of the cutaneous activity by varnishing or dipping the skin in oil causes death by asphyxia (frogs) sooner than ligature of the lungs does. **Varnishing the Skin.**—When the skin of a warm-blooded animal is covered with an impermeable varnish [such as gelatin] (*Foucault, Becquerel, Brechet*), death occurs after a time, probably owing to the loss of too much heat. The formation of crystalline ammonio-magnesian phosphate in the cutaneous tissue of such animals (*Edenhuizen*) is not sufficient to account for death, nor are congestion of internal organs and serous effusions satisfactory explanations. The retention of the volatile substances (acids) present in the sweat is not sufficient. Strong animals live longer than feeble ones; horses die after several days (*Gerlach*); they shiver and lose flesh. The larger the cutaneous surface left unvarnished, the later does death take place. Rabbits die when $\frac{1}{5}$ of their surface is varnished. When the entire surface of the animal is varnished, the temperature rapidly falls (to 19°), the pulse and respirations vary; usually they fall when the varnishing process is limited; increased frequency of respiration has been observed (§ 225). Pigs, dogs, horses, when one-half of the body is varnished, exhibit only a temporary fall of the temperature and show signs of weakness, but do not die (*Ellenberger and Hofmeister*). [In extensive burns of the skin, not only is there disintegration of the coloured blood-corpuscles (*v. Lesser*), but in some cases ulcers occur in the duodenum. The cause of the ulceration, however, has not been ascertained satisfactorily (*Curling*).]

2. **Sebaceous Secretion.**—The fatty matter as it is excreted from the acini of the sebaceous glands is fluid, but even within the excretory duct of the gland it stagnates and forms a white fat-like mass, which may sometimes be expressed (at the side of the nose) as a worm-like white body, the so-called comedo. The sebaceous matter keeps the skin supple, and prevents the hair from becoming too dry. **Microscopically**, the secretion is seen to contain innumerable fatty granules, a few gland-cells filled with fat, visible after the addition of caustic soda, crystals of cholesterin, and in some men a microscopic mite-like animal (*Demodex folliculorum*).

[**Formation of Sebum.**—The cells lining the acini of the glands proliferate and push the older cells towards the centre of the alveoli, where they undergo a fatty transformation to form the sebum. Thus the shed cells are themselves bodily transformed into sebaceous matter, a condition different to that obtaining in most of the other secretory glands.]

Chemical Composition of Sebum.—The constituents are for the most part fatty; chiefly *olein* (fluid) and *palmitin* (solid) fat, soaps, and some cholesterin; a small amount of albumin and unknown extractives. Amongst the inorganic constituents, the insoluble earthy phosphates are most abundant; while the alkaline chlorides and phosphates are less abundant.

The *vernix caseosa*, which covers the skin of a new-born child, is a greasy mixture of sebaceous matter and macerated epidermal cells (containing 47·5 per cent. fat). A similar product is the *smegma præputialis* (52·8 per cent. fat), in which an ammonia soap is present.

The *cerumen* or ear-wax is a mixture of the secretions of the ceruminous glands of the ear (similar in structure to the sweat-glands) and the sebaceous glands of the auditory canal. Besides the constituents of sebum, it contains yellow or brownish particles, a bitter yellow extractive substance derived from the ceruminous glands, potash soaps, and a special fat. The secretion of the *Meibomian glands* is sebum.

[**Lanoline.**—Liebreich finds in feathers, hairs, wool, and keratin-tissues generally, a cholesterin fat, which however is not a true fat, although it saponifies, but an ethereal compound of certain fatty acids with cholesterin. In commerce it is obtained from wool, and is known by the above name; it forms an admirable basis for ointments, and it is very readily absorbed by the skin.] Thus, the fat-like substance for protecting the epidermis is partly formed along with keratin in the epidermis itself.

3. **The Sweat.**—The sweat is secreted in the coil of the sweat-glands. At the

same time the nuclei of the secretory cells become more spherical and the cells (horse) become more granular. As long as the secretion is small in amount, the water secreted is evaporated at once from the skin along with the volatile constituents of sweat; as soon, however, as the secretion is increased, or evaporation is prevented, drops of sweat appear on the surface of the skin. The former is called **insensible perspiration**, and the latter **sensible perspiration**. [Broadly, the quantity is about 2 lbs. in twenty-four hours.]

The **sensible perspiration** varies greatly; as a rule, the right side of the body perspires more freely than the left. The palms of the hands secrete most, then follow the soles of the feet, cheek, breast, upper arm, and fore-arm (*Peiper*). It falls from morning to mid-day, and rises again towards evening, reaching its maximum before midnight. Much moisture and cold in the surrounding atmosphere diminish it, and so does diuresis. In children, the insensible perspiration is relatively great. The drinking of water favours it, alcohol diminishes it (*H. Schmid*).

Method.—Sweat is obtained from a man by placing him in a metallic vessel in a warm bath; the sweat is rapidly secreted and collected in the vessel. In this way Favre collected 2560 grams of sweat in 1½ hour [by exposing himself to a hot-air bath and drinking at the same time hot drinks]. An arm may be inclosed in a cylindrical vessel, which is fixed air-tight round the arm with an elastic bandage (*Schottin*).

Amongst **animals**, the horse sweats, so does the ox, but to a less extent; the vola and planta of apes, cats, and the hedgehog secrete sweat; the snout of the pig sweats (?), while the goat, rabbit, rat, mouse, and dog are said not to sweat (*Luchsinger*). [The skin over the body and the pad on the dog's foot contain numerous sweat-glands, which open free on the surface of the pad and into the hair-follicles on the general surface of the skin (*W. Stirling*).]

Microscopically.—The sweat contains only a few epidermal scales accidentally mixed with it, and fine fatty granules from the sebaceous glands.

Chemical Composition of Sweat.—Its reaction is **alkaline**, although it frequently is acid, owing to the admixture of fatty acids from decomposed sebum. During profuse secretion it becomes neutral, and lastly alkaline again (*Trümper and Luchsinger*). The sweat is colourless, slightly turbid, of a saltish *taste*, and has a characteristic odour varying in different parts of the body; the *odour* is due to the presence of volatile fatty acids [specific gravity, 1003–1005.] The constituents are **water**, which is increased by copious draughts of that fluid, and **solids**, which amount to 1·2 per cent. (0·70 to 2·66 per cent.—*Funke*), and of these 0·90 per cent. is organic and 0·30 inorganic. Amongst the **organic constituents** are *neutral fats* (palmitin, stearin), also present in the sweat of the palm of the hand, which contains no sebaceous glands, *cholesterin*, *volatile fatty acids* (chiefly formic, acetic, butyric, propionic, caproic, capric acids), varying qualitatively and quantitatively in different parts of the body. These acids are most abundant in the sweat first (acid) secreted. There are also traces of *proteids* (similar to casein) and a trace of *albumin* and *urea*, about 0·1 per cent. [Kast found sulphuric acid united as ethereal sulphate of skatol and phenol, also oxy-acids, and Capricana found kreatinin.] In uræmic conditions (anuria in cholera) urea has been found crystallised on the skin. When the secretion of sweat is greatly increased, the amount of urea in the urine is diminished, both in health and in uræmia (*Leube*). The nature of the reddish-yellow pigment, which is extracted from the residue of sweat by alcohol, and coloured green by oxalic acid, is unknown. Amongst **inorganic constituents**, those that are easily soluble are more abundant than those that are soluble with difficulty, in the proportion of 17 to 1; sodium chloride, 0·02; potassium chloride, 0·02; sulphates, 0·01 per 1000, together with traces of earthy phosphates and sodium phosphate. [Moreover, the relative proportion of salts in sweat is quite different from that in urine.] **Gases.**—Sweat contains CO₂ in a state of absorption and some N. When decomposed with free access of air, it yields ammonia salts (*Gorup-Besanez*).

Excretion of Substances.—Some substances when introduced into the body reappear in the sweat—benzoic, cinnamic, tartaric, and succinic acids are readily excreted; quinine and potassic iodide with more difficulty. Mercuric chloride, arsenious and arsenic acids, sodium and

potassium arseniate have also been found. After taking arseniate of iron, arsenious acid has been found in the sweat, and iron in the urine. Mercury iodide reappears as a chloride in the sweat, while the iodine occurs in the saliva.

Formation of Pigments in the Skin.—The leucocytes furnish the material, and the pigment is deposited in granules in the deeper layers, and, to a less extent, in the upper layers, of the rete Malpighii. This occurs in the folds around the anus, scrotum, nipple [especially during pregnancy], and everywhere in the coloured races. There is a diffuse, whitish-yellow pigment in the stratum corneum, which becomes darker in old age. The pigmentation depends on chemical processes, reduction taking place, and these processes are aided by light. Granular pigment lies also in the layers of prickle cells. The dark coloration of the skin may be arrested by free O [hydric peroxide], while the corneous change is prevented at the same time (*Unna*). [According to Delépine melanin is not derived from hæmoglobin, but is formed by the deep layers of the epidermis.]

Pathological.—To this belongs the formation of liver spots or *cholasma*, freckles, and the pigmentation of Addison's disease, [pigmentation round old ulcers, &c.] (§ 103, IV.). [The curious cases of pigmentation, especially in neurotic women, *e.g.*, in the eyelids, deserve further study in relation to the part played by the nervous system in this process.]

287. INFLUENCE OF NERVES ON THE SECRETION OF SWEAT.—

The secretion of the skin, which averages about $\frac{1}{8}$ of the body-weight, *i.e.*, about double the amount of water excreted by the lungs, may be increased or diminished. The liability to perspire varies much in different individuals. The following conditions influence the secretion—1. **Increased temperature** of the surroundings causes the skin to become red, while there is a profuse secretion of sweat (§ 214, II., 1). Cold, as well as a temperature of the skin about 50° C., arrests the secretion. 2. A very **watery condition of the blood**, *e.g.*, after copious draughts of warm water, increases the secretion. 3. Increased **cardiac and vascular activity**, whereby the blood-pressure within the cutaneous capillaries is increased, have a similar effect; increased sweating follows increased **muscular activity**. 4. Certain **drugs** favour sweating, *e.g.*, pilocarpin, Calabar bean, strychnin, picrotoxin, muscarin, nicotin, camphor, ammonia compounds; while others, as atropin and morphia, in large doses, diminish or paralyse the secretion. [Drugs which excite copious perspiration, so that it stands as beads of sweat on the skin, are called **sudorifics**, while those that excite the secretion gently are **diaphoretics**, the difference being one of degree. Those drugs which lessen the secretion are called **antihydrotics**.] 5. It is important to notice the *antagonism* which exists, probably upon mechanical grounds, between the secretion of sweat, the urinary secretion, and the evacuation of the intestine. Thus copious secretion of urine (*e.g.*, in diabetes) and watery stools coincide with dryness of the skin. If the secretion of sweat be increased, the percentage of salts, urea, and albumin is also increased, whilst the other organic substances are diminished. The more saturated the air is with watery vapour, the sooner does the secretion appear in drops upon the skin, while in dry air or air in motion, owing to the rapid evaporation, the formation of drops of sweat is prevented, or at least retarded. [The **reciprocal** relation between the **skin** and **kidneys** is well known. In summer, when the skin is active, the kidneys separate less **water**; in winter, when the skin is less active, it is cold and comparatively bloodless, while the kidneys excrete more water, so that the action of these two organs is in inverse ratio.]

The influence of nerves on the secretion of sweat is very marked.

I. Just as in the secretion of saliva (§ 145), **vaso-motor nerves** are usually in action at the same time as the proper **secretory nerves**; the **vaso-dilator nerves** (sweating with a *red congested* skin) are most frequently involved. The fact that secretion of sweat does occasionally take place when the skin is *pale* (fear, death-agony) shows that, when the vaso-motor nerves are excited, so as to constrict the cutaneous blood-vessels, the sweat secretory nerve-fibres may also be active.

Under certain circumstances, the amount of blood in the skin seems to determine the occurrence of sweating; thus, Dupuy found that section of the cervical sympathetic caused secretion on that side of the neck of a horse; while Nitzelnadel found that percutaneous electrical stimulation of the cervical sympathetic in man limited the sweating.

[We may draw a parallel between the secretion of saliva and that of sweat. Both are formed in glands derived from the outer layer of the embryo. Both secretions are formed from lymph supplied by the blood-stream, and if the lymph be in sufficient quantity, secretion may take place when there is no circulation, although in both cases secretion is most lively when the circulation is most active and the secretory nerves of both are excited simultaneously; both glands have secretory nerves distinct from the nerves of the blood-vessels; both glands may be paralysed by the action of the nervous system, or in disease (fever), or conversely, both are paralysed by atropine and excited by other drugs, *e.g.*, pilocarpin. In the gland-cells of both, histological changes accompany the secretory act, and no doubt similar electromotor phenomena occur in both glands.]

II. Secretory or sweat nerves, altogether independent of the circulation, control the secretion of sweat. Stimulation of these nerves, even in a limb which has been amputated in a kitten, causes a temporary secretion of sweat, *i.e.*, after complete arrest of the circulation (*Goltz, Kendall and Luchsinger, Ostroumow*). In the intact condition of the body, however, profuse perspiration, at all events, is always associated with simultaneous dilatation of the blood-vessels (just as, in stimulation of the facial nerve, an increased secretion of saliva is associated with an increased blood-stream—§ 145, A, I.). The secretory nerves and those for the blood-vessels seem to lie in the same nerve-trunks.

The secretory nerves for the **hind limbs** (cat) lie in the sciatic nerve. *Luchsinger* found that stimulation of the peripheral end of this nerve caused renewed secretion of sweat for a period of half an hour, provided the foot was always wiped to remove the sweat already formed. If a kitten, whose sciatic nerve is divided on one side, be placed in a chamber filled with heated air, all the three intact limbs soon begin to sweat, but the limb whose nerve is divided does not, nor does it do so when the veins of the limb are ligatured so as to produce congestion of its blood-vessels. [The cat sweats only on the hairless soles of the feet.] As to the **course** of the secretory fibres to the sciatic nerve, some pass directly from the spinal cord (*Vulpian*), some pass into the abdominal sympathetic (*Luchsinger, Nawrocki, Ostroumow*), through the rami communicantes and the anterior spinal roots from the upper lumbar and lower dorsal spinal cord (9th to 13th dorsal vertebræ—cat), where the **sweat-centre** for the lower limbs is situated.

The **spinal sweat-centre** may be excited **directly**:—(1) By a highly venous condition of the blood, as during dyspnoea, *e.g.*, the secretion of sweat that sometimes precedes death; (2) by overheated blood (45° C.) streaming through the centre; (3) by certain drugs (see p. 554). The centre may be also excited **reflexly**, although the results are variable, *e.g.*, stimulation of the crural and peroneal nerves, as well as the central end of the opposite sciatic nerve excites it. [The pungency of mustard in the mouth may excite free perspiration on the face.]

Anterior Extremity.—The secretory fibres lie in the ulnar and median nerves, for the fore-limbs of the cat; most of them, or indeed all of them (*Nawrocki*), pass into the thoracic sympathetic (Ggl. stellatum), and part (?) run in the nerve-roots direct from the spinal cord (*Luchsinger, Vulpian, Ott*). A similar **sweat-centre** for the upper limbs lies in the lower part of the cervical spinal cord. Stimulation of the central ends of the brachial plexus causes a reflex secretion of sweat upon the foot of the other side (*Adamkiewicz*). At the same time the hind feet also perspire.

Pathological.—Degeneration of the motor ganglia of the anterior horns of the spinal cord causes loss of the secretion of sweat, in addition to paralysis of the voluntary muscles of the trunk. The perspiration is increased in paralysed as well as in oedematous limbs. In nephritis there are great variations in the amount of water given off by the skin.

Head.—The secretory fibres for this part (horse, man, snout of pig) lie in the thoracic sympathetic, pass into the ganglion stellatum, and ascend in the cervical sympathetic (§ 356, A.). Percutaneous electrical stimulation of the cervical sympathetic in man causes sweating of that side of the face and of the arm (*M. Meyer*). In the cephalic portion of the sympathetic, some of the fibres pass into, or become applied to, the branches of the trigeminus, which explains why stimulation of the infraorbital nerve causes secretion of sweat. Some fibres, however, arise *directly* from the roots of the trigeminus (*Luchsinger*), and the facial (*Vulpian*, *Adamkiewicz*).

Undoubtedly the **cerebrum** has a direct effect either upon the vaso-motor nerves (p. 554, I.) or upon the sweat-secretory fibres (II.), as in the sweating produced by psychical excitement (pain, fear, &c.).

Adamkiewicz and Senator found that, in a man suffering from abscess of the motor region of the cortex cerebri for the arm, there were spasms and perspiration in the arm.

Sweat-centre.—According to Adamkiewicz, the medulla oblongata contains the **dominating sweat-centre** (§ 373). When this centre is stimulated in a cat, all the four feet sweat, even three-quarters of an hour after death (*Adamkiewicz*).

III. The nerve-fibres which terminate in the *smooth muscular fibres of the sweat-glands* act upon the **excretion** of the secretion.

Other conditions.—If the sweat-nerves be divided (cat), injection of pilocarpin causes a secretion of sweat, even at the end of three days. After a longer period than six days there may be no secretion at all. This observation coincides with the phenomenon of dryness of the skin in paralysed limbs. Dieffenbach found that transplanted portions of skin first began to sweat when their sensibility was restored.

Experiments on man.—If a motor nerve (tibial, median, facial) of a man be stimulated, sweat appears on the skin over the muscular area supplied by the nerve, and also upon the corresponding area of the opposite non-stimulated side of the body. This result occurs when the circulation is arrested as well as when it is active. Sensory and thermal stimulation of the skin always cause a bilateral reflex secretion independently of the circulation. The area of sweating is independent of the part of the skin stimulated.

[**Changes in the Cells during Secretion.**—In the resting glands of the horse, the cylindrical cells are clear with the nucleus near their attached ends, but after free perspiration they become granular, and their nucleus is more central (*Renaut*).]

288. PATHOLOGICAL VARIATIONS.—1. **Anidrosis** or diminution of the secretion of sweat occurs in diabetes and the cancerous cachexia, and along with other disturbances of nutrition of the skin in some nervous diseases, *e.g.*, in dementia paralytica; in some limited regions of the skin, it has occurred in certain tropho-neuroses, *e.g.*, in unilateral atrophy of the face and in paralysed parts. In many of these cases it depends upon paralysis of the corresponding nerves or their *spinal sweat-centres*.

2. **Hyperidrosis**, or increase of the secretion of sweat, occurs in easily excitable persons, in consequence of the irritation of the nerves concerned (§ 287), *e.g.*, the sweating which occurs in debilitated conditions and in the hysterical (sometimes on the head and hands), and the so-called epileptoid sweats (*Eulenburg*). Sometimes the increase is confined to *one side of the head* (*H. unilateralis*). This condition is often accompanied with other nervous phenomena, partly with the symptoms of paralysis of the cervical sympathetic (redness of the face, narrow pupil), partly with symptoms of stimulation of the sympathetic (dilated pupil, exophthalmos). It may occur without these phenomena, and is due perhaps to stimulation of the proper secretory fibres alone. [Increased sweating is very marked in certain fevers, both during their course and at the crisis in some; while the sweat is not only copious but acid in acute rheumatism. The “night-sweats” of phthisis are very marked and disagreeable.]

3. **Paridrosis** or qualitative changes in the secretion of sweat, *e.g.*, the rare case of “*sweating of blood*” (*hæmatohidrosis*), is sometimes unilateral. According to Hebra, in some cases this condition represents a vicarious form of menstruation. It is, however, usually one of many phenomena of nervous affections. Bloody sweat sometimes occurs in yellow fever. Bile-pigments have been found in the sweat in jaundice; blue sweat from indigo (*Bizio*), from pyocyanin (the rare blue colouring-matter of pus), or from phosphate of the oxide of iron (*Osc. Kollmann*) is extremely rare. Such coloured sweats are called **chromidroses**. Numerous **micro-organisms** (which, however, are innocuous) live between the epidermal scales and on the hairs, two varieties of Saccaromycetes; in cutaneous folds *Leptothrix epidermalis*, various Schizomycetes, and five kinds of Micrococci; and between the toes—*Bacterium graveolens* (*Bordoni*—

Uffreduzzi), which causes the odour of the sweat of the feet. Micro-organisms are also the cause of yellow, blue, and red sweat; the last are due to *Micrococcus hæmatodes*.

Grape-sugar occurs in the sweat in diabetes mellitus; uric acid and cystin very rarely; and in the sweat of stinking feet, leucin, tyrosin, valerianic acid, and ammonia. Stinking sweat (bromidrosis) is due to the decomposition of the sweat, from the presence of a special micro-organism (*Bacterium fetidum*—*Thün*). In the sweating stage of ague butyrate of lime has been found, while in the sticky sweat of acute articular rheumatism there is more albumin (*Anselmino*), and the same is the case in artificial sweating (*Leube*); lactic acid is present in the sweat in puerperal fever.

The sebaceous secretion is sometimes increased, constituting *seborrhœa*, which may be local or general. It may be diminished (*Asteatosis cutis*). The sebaceous glands degenerate in old people, and hence the glancing of the skin (*Rémy*). If the ducts of the glands are occluded the sebium accumulates. Sometimes the duct is occluded by black particles or ultramarine (*Unna*) from the blue used in colouring the linen. When pressed out, the fatty worm-shaped secretion is called "comedo."

289. CUTANEOUS ABSORPTION—GALVANIC CONDUCTION.—After long immersion in water the superficial layers of the epidermis become moist and swell up. The skin is unable to absorb any substances, either salts or vegetable poisons, from watery solutions of these. This is due to the fat normally present on the epidermis and in the pores of the skin. If the fat be removed from the skin by alcohol, ether, or chloroform, absorption may occur in a few minutes (*Parisot*). According to *Röhrig*, all volatile substances, *e.g.*, carbonic acid and others, which act upon and corrode the epidermis, are capable of absorption; while according to *Juhl*, such watery solutions as impinge on the skin, in a finely divided spray, are also capable of absorption, which very probably takes place through the interstices of the epidermis.

[Inunction.—When ointments are rubbed into the skin so as to press the substance into the pores, absorption occurs, *e.g.*, potassium iodide in an ointment so rubbed in is absorbed, so is mercurial ointment. *V. Voit* found globules of mercury between the layers of the epidermis, and even in the chorion of a person who was executed, into whose skin mercurial ointment had been previously rubbed. The mercurial globules, in cases of mercurial inunction, pass into the hair-follicles and ducts of the glands, where they are affected by the secretion of the glands and transformed into a compound capable of absorption. An abraded or inflamed surface (*e.g.*, after a blister) where the epidermis is removed, absorbs very rapidly, just like the surface of a wound (*Endermic method*).]

[Drugs may be applied locally where the epidermis is intact—**epidermic method**—as when drugs which affect the sensory nerves of a part are painted over a painful area to diminish the pain. Another method, the **hypodermic**, now largely used, is that of injecting, by means of a hypodermic syringe a non-corrosive, non-irritant drug, in solution, into the subcutaneous tissue, where it practically passes into the lymph-spaces and comes into direct relation with the lymph- and blood-stream; absorption takes place with great rapidity, even more so than from the stomach.]

Absorption of Gases.—Under normal conditions minute traces of O are absorbed from the air; hydrocyanic acid, sulphuretted hydrogen—CO, CO₂, the vapour of chloroform and ether may be absorbed (*Chaussier, Gerlach, Röhrig*). In a bath containing sulphuretted hydrogen, this gas is absorbed, while CO₂ is given off into the water (*Röhrig*).

Absorption of watery solutions takes place rapidly through the skin of the frog (*Guttman, W. Stirling, v. Wittich*). Even after the circulation is excluded and the central nervous system destroyed, much water is absorbed through the skin of the frog, but not to such an extent as when the circulation is intact (*Spina*).

Galvanic Conduction through the Skin.—If the two electrodes of a constant current be impregnated with a watery solution of certain substances and applied to the skin, and if the direction of the current be changed from time to time, strychnin may be caused to pass through the skin of a rabbit in a few minutes, and that in sufficient amount to kill the animal (*H. Munk*). In man, quinine and potassium iodide have been introduced into the body in this way, and their presence detected in the urine. This process is called the **cataphoric action** of the constant current (§ 328).

290. COMPARATIVE—HISTORICAL.—In all vertebrates the skin consists of chorion and epidermis. In some reptiles the epidermis becomes horny, and forms large plates or scales. Similar structures occur in the edentata among mammals. The epidermal appendages assume various forms—such as hair, nail, spines, bristles, feathers, claws, hoof, horns, spurs, &c. The scales of some fishes are partly osseous structures. Many glands occur in the skin; in some amphibians they secrete mucus, in others the secretion is poisonous. Snakes and tortoises are devoid of cutaneous glands; in lizards the "leg-glands" extend from the anus to the bend of the knee. In the crocodile, the glands open under the margins of the cutaneo-osseous scales. In birds the cutaneous glands are absent; the "coceygeal glands" form an oily secretion for lubricating the feathers. [This is denied by O. Liebreich, as he finds no cholesterol-fats in

their secretion.] The *civet glands*, at the anus of the civet cat, the preputial glands of the musk deer, the glands of the hare, and the pedal glands of ruminants, are really greatly developed sebaceous glands. In some *invertebrata*, the skin, consisting of epidermis and chorium, is intimately united with the subjacent muscles, forming a musculo-eutaneous tube for the body of the animal. The cephalopoda have *chromatophores* in their skin, *i.e.*, round or irregular spaces filled with coloured granules. Muscular fibres are arranged radially around these spaces, so that when these muscles contract the coloured surface is increased. The change of colour in these animals is due to the play or contraction of these muscles (*Brücke*). Special glands are concerned in the production of the shell of the snail. The *annulosa* are covered with a chitinous investment, which is continued for a certain distance along the digestive tract and the tracheæ. It is thrown off when the animal sheds its covering. It not only protects the animal, but it forms a structure for the attachment of muscles. In echinodermata, the eutaneous covering contains calcareous masses; in the holothurians, the calcareous structures assume the form of calcareous spicules.

Historical.—Hippocrates (born 460 B.C.) and Theophrastus (born 371 B.C.) distinguished the perspiration from the sweat; and, according to the latter, the secretion of sweat stands in a certain antagonistic relation to the urinary secretion and to the water in the feces. According to Cassius Felix (97 A.D.), a person placed in a bath absorbs water through the skin; Sanctorius (1614) measured the amount of sweat given off; Alberti (1581) was acquainted with the hair-bulb; Donatus (1588) described hair becoming grey suddenly; Riolan (1626) showed that the colour of the skin of the negro was due to the epidermis.

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